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SYMPOSIUM ON BILIARY SURGERY

Introduction to Symposium

SINCE Bobbs performed the first cholecystotomy in 1868, surgery of the biliary tract has made tremendous strides. Many of the technical advantages were made before the turn of the century: Langenbeck's cholecystectomy (1882), von Winiwarter's cholecystenterostomy (1884), Abbe's choledochostomy (1889), McBurney's duodenotomy (1892). It remained for physicians of the next century, however, to improve the diagnostic facilities, with particular reference to the Graham-Cole series in 1926, and to make surgery safer for the patient with better anesthesia and supportive care. Of special importance was the knowledge of the coagulation defect produced by vitamin K deficiency initiated by Dam in 1929 and the realization that bile was essential for the transfer of vitamin K across the intestinal wall by Greaves and Schmidt in 1937.

In spite of the many advances, biliary disease still offers many problems: Liver disease is a diagnostic challenge and its therapy leaves much to be desired; technical errors are still committed; retained postoperative common duct stones are not unusual; the treatment of acute cholecystitis is still in dispute, and cancer is an almost hopeless condition.

In order to evaluate the latest thoughts concerning these problems, the following Symposium was presented by the Third (Boston University) Surgical Service of the Boston City Hospital on April 9, 1958.

Much gratitude is due the contributors, not only for the presentation and publication of their papers but also for their personal interest in the Symposium.

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Intrahepatic Cholestasis

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INTRAHEPATIC cholestasis has been proposed as a descriptive term for biliary obstruction incident to a pathological process which originates within the liver [1]. In this state there is no change in formation of free bilirubin in the reticuloendothelial system, or its conjugation with uridine diphosphate glucuronic acid to produce bilirubin glucuronide [2]. A biochemical or morphological lesion which interferes with excretion of conjugated bilirubin by the liver cells into the bile canaliculus, its entry into the bile capillaries or transport from intralobular to interlobular to larger biliary channels may be responsible [3]. (Fig. 1.) Jaundice of this origin constitutes a major diagnostic problem as it produces clinical and laboratory features identical to those of extrahepatic biliary obstruction. These patients have cessation of bile flow with an increase in conjugated bilirubin in the serum, absent fecal urobilinogen, urinary bile without urobilinogen, an elevated serum alkaline phosphatase and hypercholesterolemia. Results of the flocculation tests and transaminases vary depending upon the cause and duration of the pathological process. A variety of histopathological lesions are seen. For study purposes we have classified our patients into three groups on the basis of the initiating clinicopathological process: (1) functional cholangiolar disease; (2) hepatocellular disease with secondary cholestasis; and (3) degeneration or atresia of the interlobular bile ducts.

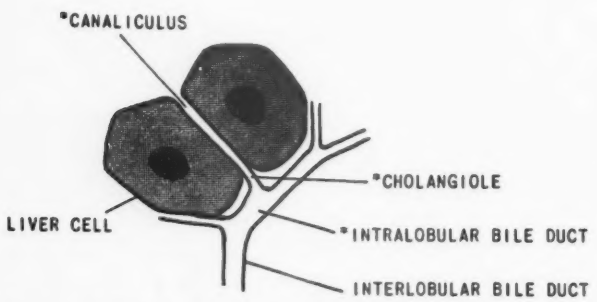

FIG. 1. Asterisk indicates site of lesions in intrahepatic cholestasis.

Functional Cholangiolar Disease. Anatomical evidence of intrahepatic cholestasis without hepatocellular alterations was first recognized as a part of epidemic or viral hepatitis [4]. Subsequently, identical lesions were described following receipt of numerous chemicals and drugs. In a group of twenty-two patients observed with protracted jaundice due to functional cholangiolar disease, chlorpromazine was responsible in nine patients [5], the virus of hepatitis in five, methimazole in two [6], methyl testosterone in two [7], and arsenicals [8], sulfonamides [9], thiouracil [10] and Nilevar® [11] in one each.

The designation functional cholangiolar disease is used as there is bile stasis without morphological alteration of the parenchymal cell or biliary network. The precise mechanism responsible for this condition is not known. It has been attributed to bile inspissation, a biochemical lesion which interferes with bile metabolism, and increased permeability of cholangioles which allows regurgitation of bile. The last postulate has received widest acceptance. According to this thesis, bile thrombi result from reabsorption of water and the encountered inflammatory reaction is due to direct effects of the noxious agent on the parenchyma.

Differentiation of functional cholangiolar disease from extrahepatic biliary obstruction depends upon making a positive diagnosis of one of these conditions or following the course of the disease. Extrahepatic biliary obstruction should be suspected with a history of biliary colic, previous gallbladder surgery or recurrent icterus; a palpable gallbladder on physical examination; roentgen criteria for cholelithiasis

or a neoplastic lesion involving the biliary tree; variations in serial biochemical tests indicating intermittent biliary obstruction; or the finding on biopsy of hydromechanical dilatation of the bile duct, bile infarcts and extravasation of bile into the portal tract [*1*]. A history of exposure to chemicals or drugs known to cause cholangiolar injury, receipt of transfusions or injections, or exposure to patients with infectious hepatitis suggests intrahepatic biliary obstruction. Chlorpromazine is the most common cause of this type of hepatitis. Icterus usually occurs two to three weeks after instituting drug therapy and is preceded by malaise, anorexia and nausea. In most instances the jaundice rapidly subsides and does not present a diagnostic problem.

Occasionally jaundice persists and available data is insufficient to establish its etiology clearly. In these instances it is often necessary to resort to surgical exploration accompanied by operative cholangiography. During the past year we have encountered five patients in whom exploration was necessary to differentiate intrahepatic and extrahepatic causes of biliary obstruction. A common duct stone was present in one of this group and a neoplasm of the head of the pancreas in another. In the other three patients, typified by a fifty-two year old housewife who had received chlorpromazine to control an acute exacerbation of nausea, vomiting and right upper quadrant distress, exploration and cholangiography revealed no extrahepatic obstruction and liver biopsy showed bile stasis as the only abnormality.

Removal of the noxious agent and supportive measures usually lead to gradual disappearance of cholestasis in functional cholangiolar disease. Adrenal steroids have been used to accelerate recovery; the often rapid decrease in icterus following steroid therapy has been used as a diagnostic aid [*12*]. Despite rest, an appropriate diet, adrenal steroids, chologogues and antibiotics, serial studies occasionally show progression of the pathologic process with ultimate development of cholangiolitic biliary cirrhosis. (Fig. 2.)

This sequence of events has been documented in patients in whom the etiological agent appeared to be a virus [*13*] as well as with chemicals [*14*]. Of our twenty-two patients with protracted jaundice due to functional cholangiolar disease, complete healing occurred in eighteen, and subsequent studies showed portal fibrosis in one and biliary cirrhosis in three.

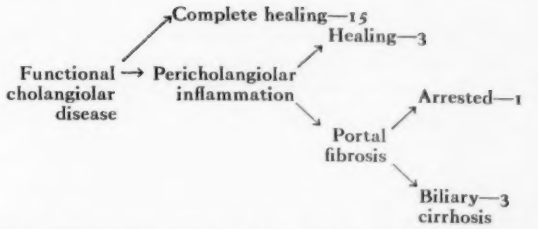

FIG. 2. Clinical course in twenty-two patients with protracted jaundice due to functional cholangiolar disease.

Unless the patient has been observed during the initial functional cholangiolar disease, a decision as to the cause of the icterus in the intermediate and terminal stages presents a more difficult problem as at this time the risk of surgical exploration is greater. Primary biliary cirrhosis is usually not accompanied by chills and fever, and this may be helpful in differential diagnosis. Hepatosplenomegaly, jaundice, xanthomas, hypercholesterolemia and hyperphosphatemia occur in cirrhosis resulting from functional cholangiolar injury and extrahepatic biliary obstruction [*15*]. Either mechanism of jaundice may produce a subacute phase characterized by pericholangiolar inflammation and portal fibrosis and an end stage with diffuse fibrosis and varying degrees of bile duct proliferation [*16*]. The following case history illustrates a progressive downhill course in functional cholangiolar disease not influenced by currently available medical therapy:

A forty-six year old housewife was hospitalized because of jaundice and pruritus. Three months previously she had received transfusions during the course of a hysterectomy. Examination revealed icterus and an enlarged liver. Biochemical study showed an elevated direct bilirubin (8.0 mg. per cent); biliuria; no urine urobilinogen; serum alkaline phosphatase, 16.0 Bodansky units; serum cholesterol, 316 mg. per cent; normal protein patterns; and a negative cephalin flocculation test. (Table 1.) Liver biopsy showed bile stasis as the only abnormality. Surgical exploration revealed a normal gallbladder and biliary tree; cholangiography showed no abnormality. Clinical and laboratory abnormalities returned to normal when the patient was given a high carbohydrate, moderate protein, moderate fat diet and ACTH was administered Two years later there was a recurrence of icterus, hepatosplenomegaly, and development of xanthomatosis and bleeding esophageal varices.

Following a portacaval shunt, despite intensive medical therapy including adrenal steroids, there was a progressive deterioration of hepatic reserve and development of hepatic coma terminally. Post-

TABLE 1
BIOCHEMICAL STUDIES IN PATIENT WITH TRANSITION OF CHOLANGIOLITIC HEPATITIS TO CIRRHOSIS

Studies	1952	1954	1956
Total bilirubin (mg. %)	8.0	8.1	12
Direct bilirubin (mg. %)	7.0	6.5	9
Alkaline phosphatase (B. U.)	16.0	8.9	29.0
Cholesterol (mg. %)	316	316	227
Cholesterol esters (mg. %)	138	171	84
Albumin (gm. %)	3.3	4.2	2.0
Globulin (gm. %)	2.8	2.4	2.1
Cephalin flocculation	Negative	Negative	Negative
SGOT (units)	.....	200	.....
Histology	Bile stasis	Portal fibrosis	Portal fibrosis

mortem examination revealed a firm, smooth, enlarged liver which weighed 1,400 gm. Microscopic sections showed moderate portal fibrosis. (Fig. 3A.)

Hepatocellular Disease with Secondary Cholestasis. An intrahepatic obstructive component is frequently present in jaundice due to hepatitis, fatty liver and cirrhosis. The obstructive element may be the major mechanism leading to jaundice in neonatal hepatitis, erythroblastosis fetalis, syphilis, galactosemia or cytomegalic inclusion body disease in infancy [*17*]; and viral hepatitis, drug intoxication, fatty liver, cirrhosis and neoplastic disease in adults [*18*]. In these instances, unlike functional cholangiolar disease, there is mechanical blockade to bile excretion, the location and type of block depending upon its cause.

In the neonatal period it is most often necessary to differentiate hepatitis and erythroblastosis from biliary atresia. Serial serum bilirubin levels may be a valuable diagnostic aid as patients with biliary atresia have progressive increase of bilirubin levels, whereas it falls in those with neonatal hepatitis or erythroblastosis. In all of these conditions the alkaline phosphatase and flocculation tests tend to be normal. Hematological studies are of principal value in establishing the presence of an Rh or ABO incompatibility as an etiological factor in erythroblastosis. It may be possible to establish a diagnosis by clinical means; however, surgical intervention with biopsy is desirable if there is uncertainty after eight weeks [*19*]. Postoperative morbidity and mortality are reduced by limiting operative procedures to biopsy and

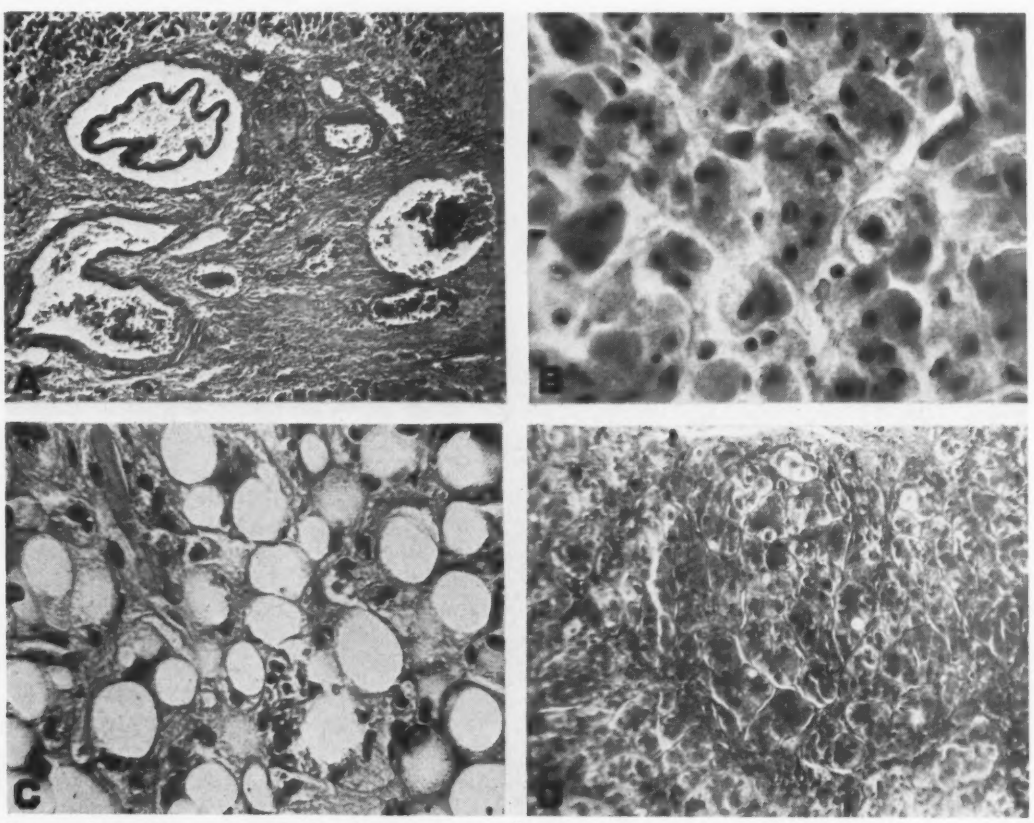

FIG. 3. A, moderate portal fibrosis. B, neonatal hepatitis showing enlarged multinucleated liver cells. C, fatty metamorphosis producing bile stasis. D, biliary cirrhosis with absence of interlobular bile ducts.

cholangiography. Extensive erythropoiesis is characteristic of the biopsy in erythroblastosis; multinucleated giant cells and inflammation are typical of neonatal hepatitis. (Fig. 3B.)

In adults viral hepatitis is the most common hepatocellular disease with secondary cholestasis. Inflammation and swelling of the parenchymal cells may occlude the bile canaliculus or other finer bile channels and thereby interfere with excretion of conjugated bilirubin. This usually occurs between the second and fourth week of the disease and may be confusing unless other features permit a correct diagnosis. Percutaneous liver biopsy may be diagnostic.

Three groups of patients exhibiting fatty metamorphosis, bile stasis, hypercholesterolemia and hyperphosphatemia, which represent stages in the fatty liver-cirrhosis syndrome, have been described: fatty liver, florid cirrhosis and diffuse septal cirrhosis [*18*]. In any of these groups bile stasis may result from compression of small bile ducts by extracellular fat. Histological study is invaluable in these patients. The following case history is illustrative:

M. H., a fifty-four year old laborer with a past history of chronic alcoholism and poor dietary habits, was hospitalized because of icterus, weakness and anorexia. Examination revealed hepatomegaly and marked jaundice without other signs of hepatic disease. Biochemical study showed a serum bilirubin of 34.0 mg. per cent; urine bile without urobilinogen; serum alkaline phosphatase, 15 Bodansky units; serum cholesterol, 567 mg. per cent; cephalin flocculation, 2 plus. A liver biopsy showed marked fatty metamorphosis with bile stasis. (Fig. 3C.) With the patient given a diet of 350 gm. of carbohydrate, 150 gm. of protein, 100 gm. of fat, 2 gm. each of choline and methionine three times daily and multivitamins, repeat studies in two months showed no clinical, biochemical or histological abnormalities and a gallbladder series was normal.

Patients with cholestasis associated with moderate to severe cirrhosis frequently present a most perplexing problem [*20*]. Often they have a superimposed obstructive lesion. Even when the hepatic disease is well documented prior to appearance of icterus, the clinical features may be baffling. Thus, in one of our patients with Laennec's cirrhosis proved by biopsy, progressive icterus developed after return to alcoholism. The jaundice and accompanying biochemical evidence of biliary obstruction was attributed to intrahepatic cholestasis but its persistence led to surgical intervention and the discovery of a pancreatic neoplasm. A similar course has been documented in four cirrhotic patients in whom a hepatoma or cholangioma developed.

Interlobular Bile Duct Degeneration and Atresia. Interlobular bile duct atresia presents a problem principally in the differential diagnosis of jaundice in the neonatal period. This condition must be differentiated at this age from extrahepatic atresia and stenosis which are amenable in some instances to surgical therapy. This diagnosis can only be established by biopsy. Closely related is the secondary development of interlobular atresia in infants with extrahepatic atresia. (Fig. 3D.) This group of patients live for longer periods, and their subsequent clinical and laboratory findings are often contradictory and confuse the clinician so that even after surgical exploration there may be a lack of clarity as to the basic mechanism responsible for icterus.

Rarely, chemical and other noxious injuries may be followed by persistent jaundice, and histological study shows no detectable interlobular bile ducts [*21*].

SUMMARY

It is now evident that a variety of medical diseases may produce intrahepatic obstruction to bile outflow. Unfortunately, in many instances it is not possible to differentiate these conditions clearly from extrahepatic biliary obstruction which requires surgical therapy. The history, biochemical liver function tests, liver biopsy and special laboratory procedures may be helpful in individual patients. Early operative exploration with biopsy and cholangiography is often desirable to eliminate the possibility of an extrahepatic obstructive lesion in patients with progressive icterus attributed to functional cholangiolar disease, neonatal hepatitis and intrahepatic bile duct atresia. Operative intervention in these conditions is poorly tolerated and an attempt should be made to minimize surgical trauma.

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DISCUSSION

John J. Byrne (Boston, Mass.): Our hospital experience has been that if we operate upon these people we have a mortality rate of about 33 per cent. We have good evidence that if you operate upon patients with liver cells that are severely damaged, as manifest by decreased cholesterol esters or elevated cephalin flocculation levels, you are going to cause death.

Rudi Schmid (Boston, Mass.): I have greatly enjoyed this paper and I think there is little to add to Dr. Leevy's excellent presentation. He has particularly emphasized the difficulties which one may encounter in deciding whether the obstruction is intrahepatic or extrahepatic; yet this decision is of the greatest importance because in cases of intrahepatic obstruction, surgical intervention may have grave consequences and postoperatively these patients often do poorly.

There are two conditions in which the diagnosis may be particularly difficult. The first is occasional cases of viral hepatitis in which the patients present with fever and occasional chills, colicky pain in the right upper quadrant and an elevated white blood cell count. Whether these patients actually have some degree of blockage in the extrahepatic bile ducts, possibly by mucus, or whether the cholestasis is entirely intrahepatic, I do not know.

Second, in cases of bilary cirrhosis, particularly in middle-aged women, it may at times be impossible to decide whether the cholestasis is due to intra- or extrahepatic obstruction. Even needle biopsy may fail to provide a definite answer. It is here that cholangiography is most valuable, as Dr. Leevy has already emphasized. It is a relatively minor procedure to make a small abdominal incision, with the patient under local anesthesia, and to put the dye directly into the cytic duct. The flow of contrast medium into the duodenum can be observed without probing or opening the common bile duct.

Dr. Leevy: That is correct.

Dr. Byrne: Have you had any experience in doing this by peritoneoscopy?

Dr. Schmid: No, I have not, but this method is used in many places with considerable success. However, it must be considered a surgical procedure, requiring sterile equipment and considerable preparation of the patient. In view of this, I believe that a small incision may be just as simple and may offer at least as much information.

Liver Decompression by Drainage of the Common Bile Duct in Subacute and Chronic Jaundice

REPORT OF SEVENTY-THREE CASES WITH HEPATITIS OR CONCOMITANT BILIARY DUCT INFECTION AS CAUSE

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THE conception of employing surgical decompression of the hepatic ductal system for relief of chronic jaundice resulting from subacute and acute hepatitis (usually of viral origin) was conceived by us many years ago when we were operating in cases of congenital atresia of bile ducts [1]. We found that atresia of the external bile ducts or obstruction due to inspissated putty-like bile in the newborn produced not only jaundice but also a marked increase of connective tissue in the liver, causing cirrhosis. This we ascribed to the irritation secondary to biliary stasis since these infants were normal except for the congenital anomaly of the bile ducts and their livers had no infection. Even in extremely pronounced cases of jaundice in which exploration disclosed a large liver, deeply pigmented, with an increased amount of connective tissue and a marked destruction of liver tissue with evidence of regeneration, we were able to establish good biliary drainage within a few days if the intrahepatic ductal system was patent.

A biliary fistula was formed by placing a catheter into the hilus of the liver proximal to the atresia. After jaundice had disappeared, secondary operations could then be performed at a later date. For one or two days the fistula would yield a thin water-clear fluid that probably represented the mucous secretion of the ducts. Due to the increased intraductal pressure, the liver cells cannot function until the pressure is relieved by intraductal drainage. After twenty-four to forty-eight hours of decompression, the bile assumes its normal color and the jaundice subsides within several weeks. Within a few months a definitive operation of the Roux Y type can be performed.

In 1955, we reported on sixty cases of liver decompression in hepatitis [2]. Since then the series has reached seventy-three cases and forms the basis for this paper.

LABORATORY TESTS

Despite the fact that after a week or two of hepatitis, the laboratory tests for liver function will not tell us the degree of concomitant involvement of the bile capillaries and intrahepatic liver ducts, we believe that surgical intervention should be more seriously considered until such tests are more discriminatory.

Many cases diagnosed from the various liver tests as due to virus hepatitis proved to be inflammatory processes of the papilla of Vater and the bile ducts, with the jaundice secondary to the inflammatory process in the bile ducts. Therefore, we believe that when virus hepatitis is not relieved within six to eight weeks and liver tests show no improvement, decompression of the liver by drainage of the common duct is indicated.

In cholangitic jaundice we have encountered three groups of patients: first, those with

severe colic-like attacks of pain; second, those without acute attacks but with mild jaundice; and third, those with deep, silent jaundice. In all three groups, the pathological condition consists of an inflammatory process in the distal portion of the common bile duct and in the papilla of Vater, producing infiltration, thickening and finally narrowing of these structures. The intensity of this process may vary; at times it may involve the entire ductal system up to the finest biliary radicals.

To illustrate how easy it is to overlook a very mild inflammation of the liver, the illness of a physician (who in several years had lost from 25 to 30 pounds and had such extreme weakness and malaise that it was even difficult for him to walk), was diagnosed as hepatitis. On examining the patient, we found tenderness over the liver, and the urine on several occasions showed traces of bile. It was quite evident that this physician had had a mild undiagnosed case of hepatitis for three years. The gallbladder was very mildly inflamed and the extrahepatic ducts showed a very mild thickening; drainage of the common duct was carried out for nine weeks. It is now five years since the operative procedure was performed and the patient is free of symptoms, has gained 35 pounds and is in excellent health.

In cases of acute and subacute hepatitis, normally due to a virus infection, the liver is usually edematous. Its color ranges from yellow to dark green. In hepatitis of longer duration but milder degree, the liver shows a marked increase in the interlobular connective tissue, which produces a picture ranging from that of a mild cirrhosis to that of a hobnailed liver. Histologically, in addition to the increase in connective tissue, there is marked vacuolation and destruction of hepatic parenchyma, which in some cases resembles a liver with subacute yellow atrophy. The pancreas varies greatly in its consistency. It can be fairly firm and lobulated or hard and diffusely swollen. There is usually a marked degree of peripancreatitis causing firm adhesions between the omentum of the lesser curvature of the stomach and the pancreatic capsule. The lesser omental cavity is often completely obliterated.

One of our patients had a severe infiltrating duodenal ulcer near the papilla of Vater that produced intermittent jaundice for a period of ten years. The clinical picture eventually indicated severe damage to the liver, with the patient stuporous. After several duodenal hemorrhages, the patient finally underwent surgery. Operation disclosed a liver about one-third normal size, with hobnailed cirrhosis, in addition to a large carbuncle-like infiltrating duodenal ulcer at the papilla of Vater. We performed high subtotal gastrectomy. For the relief of the deep jaundice that was caused by the infiltration of the papilla of Vater and the common bile duct, we anastomosed the gallbladder to the open end of the duodenum. The patient has remained well for twenty years. This case brings out two important points: (1) The liver cirrhosis was caused by an infiltrating and penetrating duodenal ulcer of long standing that produced recurrent infections and obstruction of the common bile duct resulting in intermittent jaundice. (2) After decompression of the biliary system, the liver apparently completely recovered physiologically, since the patient is in perfect health twenty years after surgery.

Another patient with a history of jaundice of five months' duration, also critically ill at the time of surgery, underwent drainage of the common bile duct. Biopsy of the liver showed marked degeneration of the hepatic parenchyma and interlobular cirrhosis. In spite of the fact that the jaundice cleared up remarkably, she died eight weeks later of acute pulmonary edema. At autopsy the liver showed areas of marked regeneration and formation of new bile ducts. This shows that even in severe cases in which the patient is critically ill, intraductal tension can be relieved.

In 1946 Watson and associates described several cases of hepatitis in which some of the patients even had attacks suggestive of gallstones, although the original history was more indicative of infectious hepatitis [3]. Biopsies of the liver at the beginning of the disease showed surprisingly little change in the liver but the subsequent attacks of jaundice over a period of several years with biopsies taken each time showed increased cirrhosis. We believe that if these patients had been subjected to decompression of the liver when the first biopsies indicated minimal hepatic changes, the probability is that the subsequent attacks would not have occurred. We refer to the patients in whom, in addition to the hepatitis, inflammation of the intrahepatic as well as of the extrahepatic bile ducts is present. It is our contention that the inflammatory process pro-

duces an obstruction of the bile flow, and the papilla of Vater does not function under these circumstances. This in turn causes an increase of the intraductal pressure which is transmitted toward the hepatic parenchyma leading to further breakdown of liver cells, necrosis, and increased jaundice. If this vicious cycle is interrupted by drainage of the common bile duct, excretion of bile will take place followed by improvement of liver function, leading eventually to complete alleviation of the jaundice. Frequently in such instances, not only is the wall of the common bile duct infiltrated and thickened but also the surrounding areolar tissue. The extreme hyperemia represented by many small blood vessels makes the identification and dissection of the common bile duct quite difficult. There is usually a large amount of bleeding from this hemorrhagic area during the dissection. In occasional cases in which the involved structures have been small, we have used special magnification eyeglasses. In many instances we were able to insert only the smallest catheter, usually employed on premature infants. A regular French catheter, with its tip cut off to insure better drainage and a good sized opening on the lateral wall of the catheter distal to where the tip was cut off, is sutured into the common bile duct, pointing toward the liver. Since such a catheter has to remain in place for nine weeks or longer, sometimes for a period of six months, we use extremely fine silk to suture the catheter into the duct. Ordinarily for one or two days, only a small amount of a colorless, watery liquid returns from the catheter, but, after this, a steady flow of bile begins, ranging at first from 60 to 90 cc., until, in the second postoperative week, 300 to 500 cc. of good normal bile is recovered in a twenty-four hour period. This is due to the relief of the intraductal pressure against the liver cells. Concomitantly, the clinical condition of the patient improves and the jaundice decreases. Tests of liver function usually return to normal within several months.

EVALUATION OF PATIENTS

Decompression was carried out in thirty-one patients with virus hepatitis. All had had jaundice for nine weeks or longer and were in poor or critical condition with several in a stuporous state. All operations were performed under local anesthesia. Four patients did not have relief of jaundice and died several months later. The other twenty-seven patients completely recovered. We will concede that some of these patients might have recovered without surgical drainage of the common bile duct; however, we believe that the recovery rate in this series could not have been attained by medical therapy alone. All these patients had had an adequate trial period of medical treatment.

Forty-two patients with subacute or chronic hepatitis due primarily to an infection of the common bile duct and the papilla of Vater underwent drainage. The ducts were thickened and infiltrated and contained a large amount of serous to seropurulent exudate. On probing the ducts there was difficulty in passing through the papilla of Vater. Patients with this type of disease as a rule recover much more quickly from their jaundice and hepatitis than those who primarily have hepatitis. In some of the longstanding cases (three to six months), the patients pass postoperatively into a phase of acute hepatitis that clinically resembles acute yellow atrophy of the liver. This happened in two cases in our series of forty-two patients in which the autopsy findings were that of an acute necrosis of the liver with acute yellow atrophy. The other forty patients recovered uneventfully.

SUMMARY AND CONCLUSIONS

Surgical decompression of the liver and its ductal system by drainage of the common bile duct (for a period of time until the patient is completely relieved) seems to be fundamental in cases of longstanding jaundice resulting from acute and subacute hepatitis, and in those cases in which the jaundice is due to primary ductal infection usually starting in the papilla and common bile duct and then extending up into the branches of the bile ducts into the liver cells. In the first twenty-four hours only clear, watery bile is secreted from the ductal epithelium, showing that the liver cells cannot function under pressure. When this pressure is relieved, bile is secreted by the liver cells, as is shown by good drainage of bile from the common bile duct catheter. Drainage of common bile duct was performed in a series of thirty-one cases of acute and subacute hepatitis with jaundice and in another series of forty-two cases of cholangitic hepatitis with jaundice. Four patients died in the first series and two in the second.

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DISCUSSION

John J. Byrne (Boston, Mass.): Thank you, Dr. Strauss. As this is a highly controversial subject, I am sure there will be much discussion.

A Doctor: Why not drain the gallbladder instead of the common duct?

Dr. Strauss: Well, in cases of cholangitis one has to perform cholecystectomy because the gallbladder is usually diseased. In cases of hepatitis, we believe that cholecystostomy does not permit adequate drainage.

A Doctor: The thing that bothers me about the whole concept is that if the obstruction is in the liver cells, how can one decompress them by choledochostomy?

Dr. Byrne: Certainly, there are two phases of the problem. One is the occasional case in which the virus inflammation spreads down and involves the common duct. You find thickened bile inside the duct, and if you open the common duct, you can relieve that aspect of the obstruction.

However, how can decompression of the common duct help the liver cell, particularly if the obstruction is up farther and you are not decompressing it? Dr. Leevy, do you have any comments?

Dr. Carroll M. Leevy (Boston, Mass.): It is our contention that the only reason for surgery is for a patient who has either functional cholangiolar disease or hepatocellular disease, but in whom hepatic obstruction could not be ruled out.

In the event one has persistent jaundice, and you operate and find there is nothing wrong with the extrahepatic biliary system, then drainage might be in order. However, there is no basic evidence to support improvement following such drainage.

We have seen 200 patients with intrahepatic obstructive jaundice. Of this group, thirty have had protracted jaundice requiring some operative intervention. Five were seen during the past year. One had a common duct stone; another had a neoplasm at the head of the pancreas. Three were typified by a fifty-two year old housewife whose cholangiograms were negative; bile stasis was the only abnormality on biopsy.

So it would be something like 15 per cent of the people seen with medical jaundice who would have an intrahepatic mechanism leading to protracted jaundice; of this group, about two-fifths would have need for actual surgical intervention.

Dr. Strauss: I do not believe, in spite of all the tests, that it is possible to have inflammation of the cells without having the same process in the capillaries and the ampulla. There is an obstructive condition of the fine bile capillaries and there is no way that you can disprove that. It is hard to conceive that the cell can be inflamed with normal bile capillary next to it.

The proof is that thirty-one patients who were in extreme stages of the disease were subjected to surgery. At operation there was found only clear, watery fluid in the bile ducts. Within twenty-four to forty-eight hours after the operations, bile started to flow and increased in amount until the normal amount was reached. The jaundice cleared up in twenty-seven of these patients and they recovered. If none had been operated upon, do you believe that these would have recovered? I do not believe so.

Tumors of the Extrahepatic Biliary System

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In 1932 Judd and Hoerner [*1*] expressed the surgical thinking of the time, in regard to extending surgery for various cancers, when they reasoned that cancers must begin locally and, if detected early and completely removed, cure is possible. This philosophy has been the guiding light of an era of wider and wider resections up to the limit of survival of the patient, an era which is ending in terms of technical improvement. The two basic tenets of this philosophy have been early diagnosis and complete removal. While attempts at complete removal have reached natural limitations, there has been no corresponding advance toward earlier diagnosis. Thus, as with cancer of the breast, stomach, lung, colon, and pelvic organs, the difficulty of early diagnosis is the greatest limitation to successful treatment.

For practical purposes, benign and malignant tumors of the hepatic ducts, common bile duct, gallbladder, papilla of Vater, and head of pancreas may be considered together because of their anatomical proximity, symptoms, clinical course, and methods of treatment.

BENIGN TUMORS

Benign tumors are important because they may simulate malignant tumors in the manner of onset of symptoms and in gross appearance. Benign tumors are clinically rare and are, usually, discovered accidentally at laparotomy or because they cause obstructive jaundice; they are adequately treated by local excision or fulguration [*2*]. There are certain nonneoplastic lesions which are encountered frequently and may be misleading. The so-called papilloma of the gallbladder is usually an aggregation of cholesterol crystals which appears as a fixed filling defect on cholecystogram and may be multiple. Benign leiomyomas and cholesterosis of the gallbladder with deep Rokitansky-Aschoff sinuses may appear as fleshy tumors. (Fig. 1.) A stone impacted in the distal common duct with regional edema and fibrosis may simulate a carcinoma of the head of the pancreas or duodenal papilla. Chronic pancreatitis of the head of pancreas may be indistinguishable from carcinoma. Adequate biopsy is therefore essential before a radical operation is performed.

MALIGNANT TUMORS

My chief concern in this report is with malignant tumors, their diagnosis and the results of treatment. It is worth while examining the type and duration of symptoms since it is only through them that earlier diagnoses may be made. Abstracted for this purpose are the charts of 229 patients with carcinoma of the extrahepatic biliary system including the head of the pancreas, seen at the Cleveland Clinic from 1946 through 1955. The occurrence of symptoms consistently present is analyzed in Table 1.

There was a predominance of males except in that group having carcinoma of the gallbladder. Jaundice and pain were of equal incidence in carcinoma of the head of the pancreas. This was also true for carcinoma of the gall-

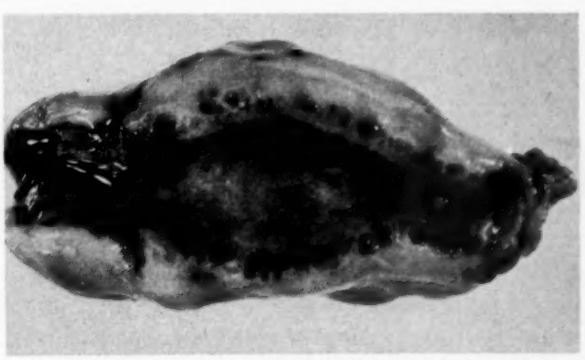

Fig. 1. Grossly hard nodular gallbladder with cholesterosis and deep Rokitansky-Aschoff sinuses.

Table I

Lesion	♂	♀	Jaundice No.	Jaundice Mean Duration Mos.	Pain No.	Pain Mean Duration Mos.	Fever No.	Fever Mean Duration Mos.
			SYMPTOMS					
Head Of Pancreas 182	108	54	72	1.8	102	4.2	3	1.5
Gallbladder 25	4	21	14	1.7	18	2.8	0	0
Papilla 20	16	4	18	4.1	4	7.5	5	3.8
Hepatic Duct 14	7	7	13	1.6	4	2.3	0	0
Distal Common Duct 5	3	2	5	2.4	1	2.0	0	0
Cystic Duct 3	2	1	3	1.0	1	0.5	0	0

bladder but pain was usually associated with stones and colic. Gallstones were present in 80 per cent of these patients. A recent interesting discussion of the relationship between gallstones and carcinoma of the gallbladder reviews the similarity between bile acids and carcinogenic agents [3]. Jaundice was the most common presenting symptom for ductal and ampullary lesions. Fever was uncommon and was apparently due to cholangitis or cholecystitis.

Delay in diagnosis and laparotomy was preponderantly due to prolonged symptomatic treatment of vague upper abdominal distress. A recent increase in severity of chronic pain or the appearance of jaundice were the two symptoms which usually brought the patient to a physician. A mean period of duration of jaundice of 2.1 months was due largely to patient apathy, a mistaken diagnosis of hepatitis, and repeated attempts at "biliary flush."

Collateral symptoms of recent and chronic weight loss, anorexia, vague epigastric distress and intolerance to fat were present in most patients in greater or lesser degree. Weight loss appeared related to voluntary reduction in dietary intake to avoid discomfort except with carcinoma of the pancreas, although steatorrhea was uncommon. A palpable mass proved to be a distended gallbladder with carcinoma of the ampullary region or a large mass in the head of the pancreas with carcinomatosis in 95 per cent of the cases.

The preoperative diagnosis in 80 per cent of patients presenting with jaundice was common duct stone; 15 per cent had had previous cholecystectomy. Most patients with pain alone had carcinoma of the pancreas and were studied by upper gastrointestinal series. In every patient in whom the "reverse E" sign was present in the second portion of the duodenum, laparotomy disclosed widespread cancer. Desquamatory cytology from duodenal drainage, retrograde cholangiogram through double ballooned duodenal tube, intravenous cholangiography, and reliance upon guaiac positive stool or duodenal drainage were all tried and found unpredictable. In brief, during the past twenty-five years we have not improved diagnostic methods except to have a higher clinical suspicion of neoplasm. Wider experience with duodenal drainage cytology seems to have the most promise potentially. In the absence of evidence of liver failure or hepatitis, a history of recent treatment with chlorpromazine or methyl testosterone, or evidence of a hemolytic process, patients with jaundice should undergo exploration as soon as they can be prepared.

OPERATIVE DIAGNOSIS

In 87 per cent of the 229 patients with tumors in this region, the diagnosis was grossly obvious at operation. A gross lesion with peritoneal seeding and enlarged regional nodes was, unfortunately, the common operative finding.

The following are gross indications that, although resection may be possible, little chance for cure exists: (1) grossly involved nodes high in the porta hepatis; (2) fixation to portal vein or mesenteric vessels; (3) gross penetration of the pancreatic capsule with local satellite lesions; (4) gross metastasis to the liver; and (5) involved nodes adjacent to the primary lesion with *extensive edema regionally*.

It seems axiomatic that cancer of the gallbladder was either completely unsuspected by the surgeon (Fig. 2) or was grossly obvious, e.g., the unusual fibrosarcoma shown in Figure 3. Attempts at wide local excision when cancer has been grossly recognized has not improved survival rate.

A normal appearing ductal system in a patient with jaundice, with no bile present in the common bile duct, proved to be carcinoma of the intrahepatic ducts in eight cases.

Operative diagnosis of less conspicuous and, theoretically, more favorable carcinomas of distal common duct, duodenal papilla, and head of pancreas depends more upon confirmation by histologic frozen section than upon palpation. Differentiation from impacted stone, benign tumor, and chronic pancreatitis will avoid radical resection. Transduodenal needle

FIG. 2. Gross chronic cholecystitis with cholelithiasis. Carcinoma discovered on microscopic study. Patient died with metastases six months after secondary excision of bed of gallbladder.

biopsy offers the least opportunity for seeding implantable cancer cells. At this juncture, a decision must be made whether to stage the operation by creating a biliary by-pass and allowing the liver to recover from jaundice of weeks' or months' duration, or to proceed with the one-stage radical resection. A decision for

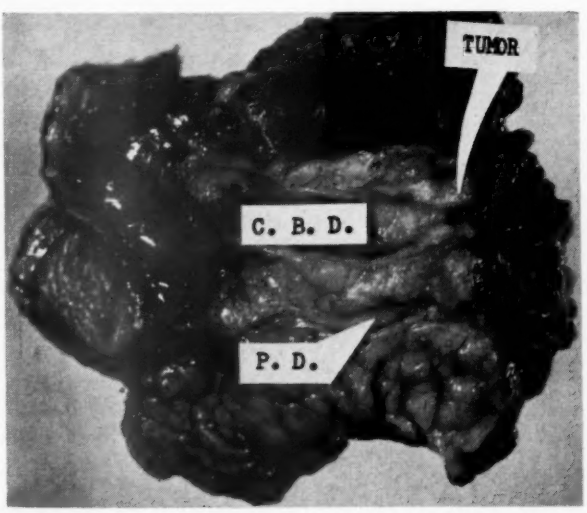

FIG. 4. Small carcinoma of distal common duct without involved nodes. The common bile duct (C.B.D.) and pancreatic duct (P.D.) are indicated. Patient died forty-six months postoperatively with widespread metastases.

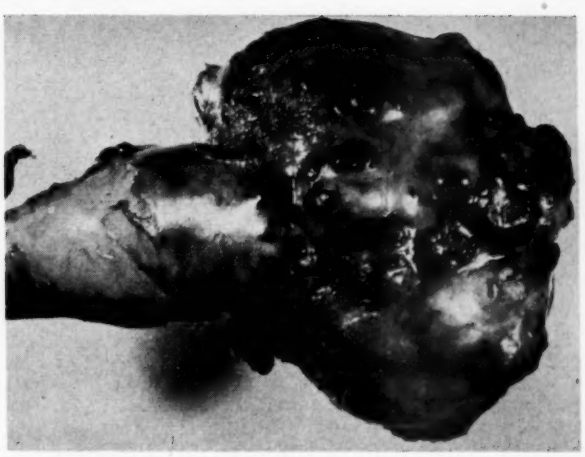

FIG. 3. Fibrosarcoma of gallbladder presenting as pelvic mass. Patient died with metastases ten months following grossly complete removal.

radical resection depends upon gross evidence that the neoplasm is still localized. Grossly, the lesions illustrated in Figures 4, 5, 6 and 7 were thought favorable for complete removal yet only one (Fig. 7) has been apparently cured.

TECHNIC

The various steps in the evolution of radical pancreaticoduodenectomy probably begin with Halsted in 1899 [4] when he successfully performed a local resection of a portion of pancreas, duodenum, and common duct and implanted pancreatic and bile ducts into the duodenal line of anastomosis. A cholodochostomy was necessary for stricture at three months and the patient died with metastasis at six months.

During the next thirty-six years anastomosis leaks, bile peritonitis, hemorrhage, and pan-

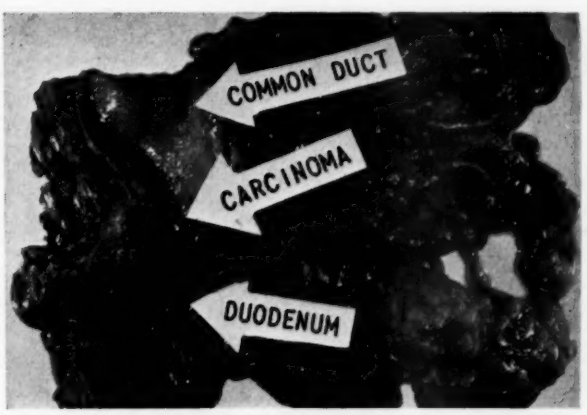

FIG. 5. Small carcinoma of the distal common duct. Patient died twenty-two months after operation with large hepatic metastases.

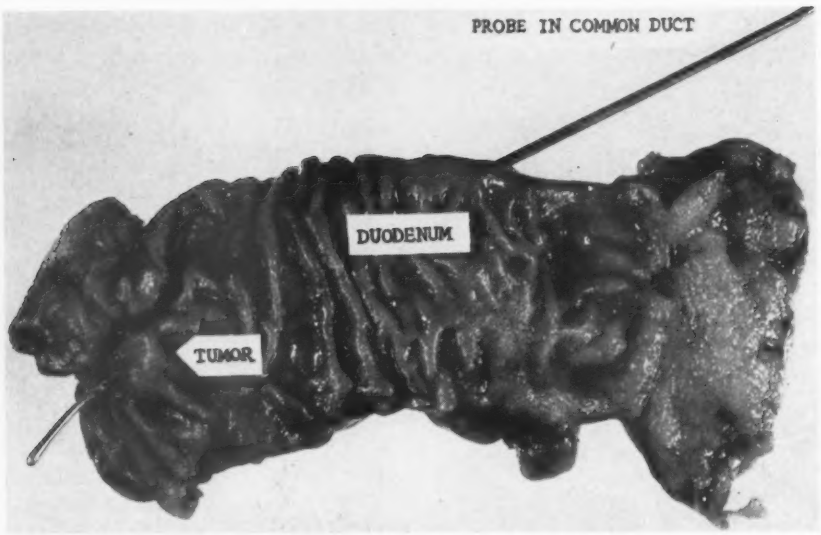

FIG. 6. Infiltrating carcinoma of duodenal papilla with microscopically involved regional nodes. Patient survived six months.

creatitis took a heavy toll but in 1922 Tenani [5] obtained a five-year survival for a patient with an ampullary lesion by extended local resection and duct implantation. Several things plagued the surgeon during this period. It was believed that pancreatic secretions were essential to life and every attempt was made to implant the duct. With absorbable suture material digested away by pancreatic enzymes, leaks and peritonitis killed those who had not died from hemorrhage due to vitamin K deficiency. Progressive liver failure associated with biliary cirrhosis frequently followed surgery.

In 1935 Whipple and associates [6] reported a two-stage operation, the first stage of which by-passed biliary obstruction and allowed the damaged liver to recover and coagulation to return to normal. The second stage weeks or months later involved resecting *en bloc* the entire duodenum, distal stomach, head of pancreas, common bile duct, and implanting bile and pancreatic ducts. Later, the discovery that pancreatic secretion is not essential to life encouraged them to close the pancreatic stump and the incidence of leaks diminished.

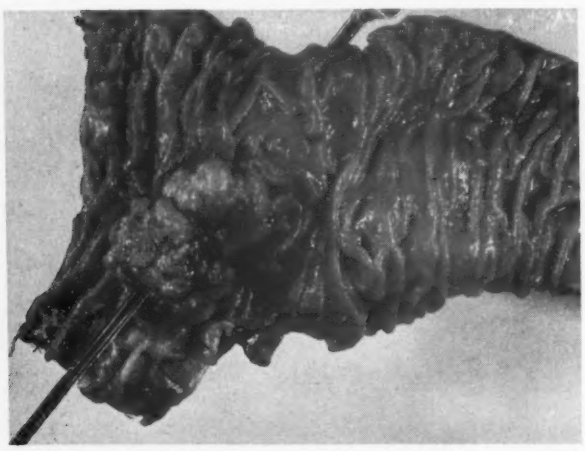

FIG. 7. Bulky papillary carcinoma of the ampulla without involved regional nodes. Patient is alive without evidence of recurrent cancer five years after operation.

In 1937 Brunschwig [7] reported the first successful radical resection without implantation of the pancreatic duct for cancer of the pancreatic head.

By 1940 Quick [8] and others demonstrated the role of vitamin K in coagulation and vitamin K was available to correct the prolonged prothrombin time preoperatively. In 1941 Whipple [9] reported success with a one-stage operation and since then there have been only minor variations in technic.

The high incidence of ascending cholangitis following cholecystogastrostomy has led to other measures for biliary drainage [10]. The finding of free cancer cells in pancreatic ducts [11] and periductal infiltration into the pancreas]12[have been shown as evidence that total pancreatectomy should be performed for lesions of the head of pancreas. Infiltration of lymphatics along the common bile duct suggests that transsection should be at the hepatic duct level and the gallbladder included in the *en bloc* specimen [13].

The operation in most clinics today consists of *en bloc* removal of the distal part of the stomach, the entire duodenum, gallbladder and common duct, the head or total pancreas, and nodes along the common hepatic duct and gastroduodenal vessels.

Reconstructions follow the general patterns shown in Fig. 8 with implantation of the pancreatic stump carried out to prevent steatorrhea. A useful maneuver, since the non-obstructed pancreatic duct may be very small, is to cannulate it with a rubber tube which is brought out through the wall of jejunum and abdomen to provide external drainage during the period of healing.

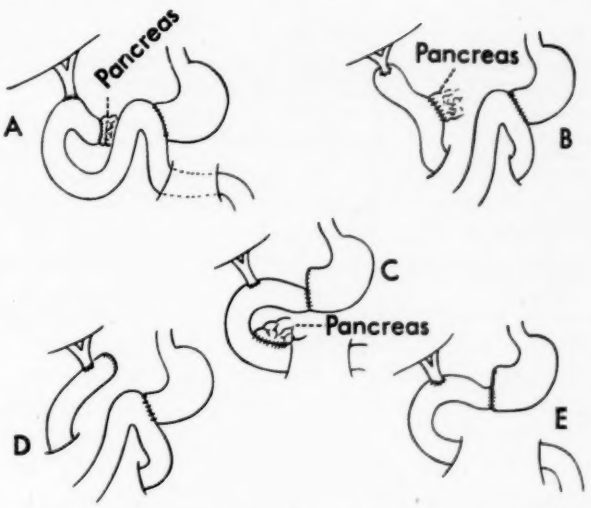

FIG. 8. Common methods of reconstruction after radical pancreaticoduodenectomy. Methods (D) and (E) are used after total pancreatectomy.

RESULTS

In this country, out of several hundred reported attempts at cure by radical surgery for carcinoma of the head of pancreas, there are fewer than twenty-five patients who have survived five years or more and 20 per cent of these had recurrent tumor. For carcinoma of the duodenal papilla and distal common bile duct, there are reported about fifty five-year survivors with approximately 15 per cent having recurrent disease. There are in the neighborhood of twenty patients who have survived ten years or more and are apparently cured. The cure rate for cancer of the gallbladder is about 2 per cent and most of these lesions have been of the carcinoma *in situ* variety. There are even fewer long-term survivors with lesions of the cystic duct or proximal common duct, and none reported with lesions of the hepatic ducts.

Table II is a breakdown of the 229 cases explored during a ten-year period ending in 1955. These results are comparable to those reported from similar institutions in recent years. The over-all survival time following radical and palliative operations was approximately the same. All but three patients lost to followup had gross or pathological evidence of residual carcinoma. These three had carcinoma of the pancreas and margins of resection free from tumor but had involved nodes in the resected specimens. Two patients had carcinoma *in situ* of the gallbladder, treated by cholecystectomy only, and are alive twelve and twenty-nine months later, clinically cured.

The single survivor for five years had a favorable lesion of the ampulla without involved nodes in the specimen.* The relatively favorable exophytic variety of tumor (Fig. 7) has been noted by several authors.

Tables III and IV, analyzing the causes of

* Patient operated upon by Stanley O. Hoerr, M.D.

Table II

Lesion		SURGICAL RESULTS No.	Op. Mort.	Def. Group	0-6 Mos.	6-12 Mos.	12-18 Mos.	18-24 Mos.	>24 Mos.	? Cure
Head Of Pancreas 162	P	152	8.5%	72	56	9	5	2	36d	
	R	10	20%	4	2	2	0	0	0	
Gallbladder 25	P	24	12.5%	18	13	4	0	0	29L	1
	R	1	0	0	0	0	0	0	0	
Papilla 20	P	5	20%	4	2	0	0	1	33d	
	R	15	33%	6	2	0	1	1	48d 60L	1
Hepatic Duct 14	P	14	14%	8	0	5	2	1	0	
	R	0	0	0	0	0	0	0	0	
Distal Common Duct 5	P	3	0	3	0	2	0	0	40d	
	R	2	50%	0	0	0	0	0	0	
Cystic Duct 3	P	1	0	1	1	0	0	0	0	
	R	2	0	2	0	1	0	0	27d	

Table III

Lesion	OPERATIVE MORTALITY Mean Age ♂	♀	Op. Mortality (%)	Cause Operative Death
Head Of Pancreas 162	58	52	9	1 pulmonary embolus, 8 days 2 cardiac failure, 1 day 1 cardiac arrest 1 coronary occlusion, 2 days 1 cerebral accident, 21 days 1 shock, 1 day 3 bile peritonitis, 7,14, 21 days 1 ruptured abdominal aneurysm 2 days 3 carcinomatosis, 3,6,18, days
Gallbladder 25	67	60	12	1 pneumonia, 6 days 1 shock, 7 days 1 uremia, 14 days
Papilla 20	61	62	30	4 bile peritonitis, 14,17,19, 21 days 1 cerebral accident, 30 days 1 pancreatitis, 30 days

Table IV

Lesion	OPERATIVE MORTALITY: Mean Age ♂	♀	Op. Mortality (%)	Cause Operative Death
Hepatic Duct 14	59	57	14	1 bile peritonitis, 1 day 1 carcinomatosis, 14 days
Distal Common Duct 5	62	67	20	1 hemorrhagic shock, 1 day
Cystic Duct 3	47	59	0	0

operative mortality, indicate an over-all mortality of 10 per cent for palliative operations and 27 per cent for radical operations. The majority of fatalities occurred during the period from 1946 through 1951 and the mortality for radical operation since 1955 has been 0 per cent in six cases. Planned use of the two-stage operation in badly depleted patients with jaundice seems to have contributed to the reduction of operative mortality.

COMMENTS

It is obvious that improved results can be obtained in only two ways: (1) *earlier diagnosis and operation;* and (2) *reduction of operative mortality*.

With an average mortality from 15 to 20 per cent and long-term survivors less than 10 per cent for pancreatic cancer and less than 30 per cent for ampullary lesions, are we justified in continuing extended radical surgery for carcinoma of the extrahepatic biliary tract in cases which appear favorable?

In 1949 Cattell and Pyrtek [*11*] wrote: "In the light of our present experience, we must modify the operative procedure or abandon radical surgery for carcinoma of the head of the pancreas. While many of these patients have a smooth recovery and are quite comfortable for a number of months, the duration of life following resection hardly justifies such a major procedure, since satisfactory palliation might have been procured by a side-tracking procedure such as cholecystojejunostomy."

In 1951, Parsons [*12*], reviewing Whipple's series, wrote that the results of radical surgery were disappointing and that by-passing operations were indicated for any visible or palpable evidence of spread of the disease.

However, in 1952 Brunschwig [*14*] wrote: "At the operating table, in the presence of a stony hard mass in the head of the pancreas, the surgeon has to make up his mind. He cannot delve into the philosophy of it and wonder how long his patient might live if he closed up, and what his justification would be to go ahead. When we are faced by one of these tumors that does not have peritoneal dissemination, with no evidence of liver metastasis, we are obliged to take it out or say at the outset that we will do only short-circuiting procedures. One should not devise excuses for not going ahead and doing the operation when the tumor is resectable simply because it is in the head of the pancreas."

In 1957 Rhoads, Zintel and Helwig [*15*] wrote: "We believe that radical pancreaticoduodenectomy is worth while in the more favorable cases of pancreatic-duodenal carcinoma and that efforts should be focused on lowering the operative risk."

CONCLUSION

With cancer of the extrahepatic biliary structures, as with extended radical surgery for cancers of other regions of the body, consideration must be made of the operative toll of life and the social usefulness and well being of patients subjected to such surgery. Consideration must be made of the surgeon and his competence to decide and carry out the operation. Consideration must be made of the fact that at present radical surgery offers the only chance for cure.

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DISCUSSION

DR. JOHN J. BYRNE (Boston, Mass.): Dr. Britton has raised many interesting points. Dr. Brunschwig's name was taken in vain several times. I wonder if he would like to start the discussion?

DR. ALEXANDER BRUNSCHWIG (New York, N. Y.): I want to say that I enjoyed Dr. Britton's presentation very much. I think that he aptly summarized the situation and I agree essentially with everything that he said.

There is too much being made of this idea that there is a controversy between those who believe in radical surgery and those who do not. Fundamentally, everybody wants to help the patient.

We are in no position to make stereotyped rules, but I certainly agree fundamentally with what Dr. Britton said. I believe that the results are poor, but in the meantime, what are we going to do? Until we get something better than we have, those interested in surgery of cancer will have to be satisfied with what we have now.

DR. BYRNE: What are your survival rates?

DR. BRUNSCHWIG: Frankly, to me, percentages of five-year survivals in this sort of thing mean very little, because I see a lot of patients whom you open and close. Now, we have six five-year survivors from cancer in the pancreatic and duodenal region. What percentage that is, I do not know.

I see a lot of patients who are not operable to begin with, and if I put all of those into the group, then the figures are ridiculously small.

A DOCTOR: I wish to compliment Dr. Britton for the fine paper he presented. I am sure that his remarks reflect the experience of those who have been working on these cases.

I should like to emphasize Dr. Britton's plea for early diagnosis. For instance, if you take more interest in the patient with indigestion and dyspepsia, you might get more of the patients Dr. Brunschwig spoke of in the salvaged group.

DR. BYRNE: Would Dr. Dunphy like to comment on the problem of biopsy?

DR. ENGLEBERT DUNPHY (Boston, Mass.): I would say that if I could get an adequate biopsy through the duodenum, and our Pathology Department would give us a firm report, I would be willing to do it, but our experience has not been entirely happy.

We have had the experience of getting a repeated diagnosis of chronic pancreatitis on biopsy and yet, with a firm clinical conviction that it was neoplasm, resecting it, and finding it to be cancer on final sections. I have also resected what was thought to be wholly benign, chronic pancreatitis, but found cancer on multiple sections.

Therefore, I personally think I have to rely on what I find at operation. However, ampullary lesions are a different matter since one can make a pretty firm decision before doing the resection.

Unfortunately, the vast majority of patients are not going to be cured by evidence that is clear to the surgeon when the abdomen is opened; there is a small group in which one surgeon will abandon the procedure but another will attempt a more heroic procedure. This is an individual matter that has to be settled by the surgeon at the operating table in his own best judgment.

DR. BYRNE: Has anybody in the group any experience with the modified or unmodified Longmire procedure in people who have inoperable carcinoma of this type? We know that Dr. Child has several six-to-eight-month survivals.

DR. BRUNSCHWIG: It is a method for clearing the jaundice temporarily and it works.

Hepatic Lobectomy

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RESECTION of hepatic tissue as a planned procedure was first carried out in 1888 by Langenbuch [1]. The first planned right hepatic lobectomy was performed by Wendel [2] in 1911. There are over 1,000 references in the literature to hepatic tissue resections for neoplasms of various types; however, until the present time no one surgeon has had a great deal of personal experience. I [3] have carried out over seventy-five excisional procedures upon the liver for varying types of neoplasms, of which a total of thirty-four have been lobectomies. Twenty were right hepatic lobectomies and fourteen were left hepatic lobectomies.

It would appear that two factors have been regarded as especially dangerous in connection with surgery of the liver in the past: (1) hemorrhage, and (2) infection. When incised, the liver parenchyma oozes blood at first vigorously; but if large vessels are clamped, the weeping of blood from the parenchyma soon may be arrested by continued pressure with dry gauze or gauze sponges soaked in hot saline solution. As to infection, the human liver, in contrast to that of the dog, is sterile and therefore there is no greater danger of infection than in other operations upon abdominal viscera.

Small tumors may be excised by encompassing elliptical incisions and sharp dissection. Tumors near a margin of the liver may be removed by excision of a wedge-shaped portion of the parenchyma to include the growth. In both instances, after the excision, pulsating arteries and bleeding veins are clamped and ligated. Large bile ducts are likewise secured and ligated. The freshly cut surfaces are approximated by interrupted catgut sutures which are placed to include generous portions of liver parenchyma. A cardinal principle of such surgery is the placing of soft rubber drains to the operative sites to facilitate escape of bile should this occur during the immediate postoperative period. It almost always occurs, but I have never observed a permanent biliary fistula resulting from partial hepatectomy. Neoplasms which bulge outward from one of the margins of the liver and have some sort of pedicle may be removed by transection of the pedicle. The raw surface is compressed by a row of interlocking interrupted mattress sutures. The latter serve for hemostasis and compression of the transected bile ducts.

The entire right or left lobe of the liver may be resected. Two methods are possible. The one, a guillotine type of liver lobectomy, consists of vertical transection of the lobe just to the right or left of the falciform ligament as the case may be, leaving a 1 or 2 cm. layer of liver tissue at the base of each lobe. In this type of excision great care must be exercised to secure the large blood vessels and bile ducts as the transection progresses. In regard to the left lobe, place the index finger of the left hand on the upper surface of the left lobe just to the (surgeon's) right of the falciform ligament and the left thumb on the undersurface. Compression of liver parenchyma between these two digits is exerted prior to incision of the liver itself. As large arteries, veins and bile ducts are encountered during the progressive transection by repeated shallow strokes of the scalpel, they are clamped and ligated. The left hepatic vein should be identified and doubly clamped before it is divided and the operation terminated by removal of the left lobe. For the right lobe the same principle may be followed, using the right thumb and index finger applied just to the left (surgeon's) of the falciform ligament. Because the right hepatic vein is quite large, considerable care is to be exercised in securing it prior to transection. Leaving a small pyramidal portion of liver parenchyma of the right upper lobe adjacent to the falciform ligament in order

to ligate by transfixation sutures may facilitate right lobectomy without the hazard of exposing the right vein. In total right hepatic lobectomy the gallbladder is also removed *en masse* with the right lobe. Prior to transection of the base of the right lobe the cystic duct is exposed, doubly ligated and transected. The cystic artery is also divided and ligated. The gallbladder is left attached to the liver. The caudate lobe of the liver may or may not be removed separately; it has its own group of vessels which must be dealt with.

In 1936 Huard and Meyer-May [4] described the procedure of detaching (except for division of the left hepatic vein) the left lobe by vertical incision just to the left of the falciform ligament and then isolation and ligation of the left branch of the portal vein, left branch of the hepatic artery and left branch of the common bile duct, and finally division of the left hepatic vein. In regard to the right lobe, Lortat-Jacob and Robert [5] described what they refer to as controlled right hepatic lobectomy. This consists of exposure by means of a right thoracoabdominal incision starting over the right eighth rib at its angle, and division of the diaphragm to the vena cava. The round and triangular ligaments of the liver are divided and the liver retracted upward into the thorax. The cystic duct, cystic artery and right branches of the hepatic artery and right hepatic duct are transected. The liver is then luxated downward and forward to the left in order to secure and divide the right hepatic veins. The base of the right lobe of the liver is then cut through just to the right of the falciform ligament. The raw surface is covered with falciform ligament.

The following is a summary of the author's experience with hepatic lobectomies:

Simple Right Hepatic Lobectomy. There were two cases of massive angioma. Both patients are living and well seven and six years later, respectively.

Five cases were primary hepatic malignant hepatomas. Two patients died following surgery; one lived for two years and died of recurrences. Two patients are living and well, each six years after operation.

There were seven cases of metastatic carcinoma from previously resected primary lesions in the colon (six cases) and uterus (one case). Three patients died following surgery, and the other patients lived up to fourteen months, receiving various degrees of palliation mainly in the form of pain relief.

Complex Right Hepatic Lobectomy, i.e., right hepatic lobectomy and in addition partial pancreatoduodenectomy or partial left hepatic lobectomy, or right colectomy. There were five cases of carcinoma of the gallbladder invading the porta hepatis and upper margin of the head of the pancreas. All patients died following surgery.

There was one case of carcinoma of the gallbladder invading the porta hepatis and upper margin of the head of the pancreas. The patient is living and is clinically well but now has recurrences.

Left Hepatic Lobectomy. Two patients underwent left hepatic lobectomy in conjunction with radical gastrectomy for cancer of the stomach. One patient lived over seventeen years; one lived one year.

In two cases left hepatic lobectomy was performed in conjunction with resection of gastric stumps and loops of jejunum for recurrent gastric cancer. Both patients survived about six months.

Eight patients underwent left hepatic lobectomy for metastatic cancer from colon, uterus, breast. Survival varied from six to twenty-three months. There were two surgical fatalities.

One patient with cholangio-carcinoma lived eighteen months.

One patient with primary angiosarcoma is living and well nine months after surgery.

OPERATIVE MORTALITY

Procedure	No.	%
Simple total right hepatic lobectomy	5 of 14	36
Complex total right hepatic lobectomy	5 of 6	83.3
Total left hepatic lobectomy	2 of 14	15

Four patients are living more than five years after total right hepatic lobectomy; two had had massive angiomas and two had had primary hepatic cell carcinomas. One patient lived over seventeen years following left hepatic lobectomy in conjunction with radical gastrectomy for cancer of the stomach.

COMMENTS

It has long been known that about 80 per cent of the liver may be resected in animals, with survival. My experience with right

hepatic lobectomy and survival for five or more years of some of these patients with only the left hepatic lobe remaining amply confirm earlier observations on lower animals as applied to this situation in man. Physiological studies on patients reveal no special relationships between the presence of tumor (primary or secondary) and hepatic physiological aberrations due to the tumor *per se* [6,7]. Of course neoplasms in the presence of cirrhosis pose a different question. Certain forms of cirrhosis may predispose to diffuse cancerization of the liver, as for example the high incidence of diffuse hepatic cancer in the Bantus, in whom diffuse cirrhosis develops in early life due presumably to nutritional deficiencies. Because of the diffuse nature of such hepatic neoplasms, no surgical problem is posed.

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DISCUSSION

Chairman Byrne: Dr. Brunschwig, you certainly have shown some very brilliant results. Does anybody want to discuss this paper?

A Doctor: I can only rise to a point of order to congratulate somebody who has to offer as many cases of lobectomy as Dr. Brunschwig.

Technic of Cholecystectomy

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MANY operations are perhaps more difficult from a technical point of view than cholecystectomy but there are few in which the margin of safety is as small and where a false move of perhaps .5 cm. or less can lead to such terrible consequences, e.g., injury to the bile duct. Any surgeon having had experience with even one such patient or, worse still, having produced one such result has certainly been impressed far beyond the effect of any word picture that might be drawn.

There is nothing new in the technic of safe removal of a gallbladder. The same old tried and true standard precautions are as good as they ever were, and if followed are as rewarding as they always have been. Lahey [1], who has written and been quoted extensively on this subject, has said, "We should publicize the fact that cholecystectomy is a dangerous operation. It is dangerous unless one realizes how important it is to control the blood supply, to demonstrate definitely the anatomic relationships and to realize that anomalous anatomy is very common. I believe that we could do nothing better than to write more and more on the need for accuracy in cholecystectomy."

There is often difficulty in obtaining hemostasis during cholecystectomy. Bleeding may occur in a deep hole, with perhaps poor light and inadequate relaxation. In such a situation an inexperienced or even an experienced operator, if not alert, may damage the ducts in a hasty attempt to control a bleeder. Speaking of injuries to the duct in this vein, Lahey [2] has said, "They are the result of excitement, I think. The cystic artery gets loose, bleeds into the deep operative field. The inexperienced operator fails to realize that by pinching the hepatic artery with his fingers he can stop the bleeding artery, wipe the field dry, find the bleeding vessel and control it accurately. Instead of this he clamps wildly and picks up the hepatic duct in the clamp." First, there must be good anesthesia with adequate relaxation. Second, one must have an adequate incision, enlarged as the operation progresses if need be, good lighting and a good assistant. It is a good routine to orient oneself to the foramen of Winslow after exposure and proper retraction have been obtained, and to locate the hepatic artery between the thumb and forefinger. This takes only a few seconds and may prove invaluable later on.

The type of incision is not important. I am partial to the subcostal incision for I believe this produces less discomfort postoperatively and there is a lesser incidence of hernia and perhaps dehiscence. It has the disadvantage of making it difficult or impossible to remove an occasional appendix at the same time. The type of incision is not important so long as it is large enough to let you see plainly what you are doing and to allow your assistant to assist you.

I am not going to discuss the pros and cons of whether a gallbladder should be removed from above downward or whether the dissection should start from below. I frequently remove acutely diseased gallbladders from above downward when there is a great deal of reaction around the ducts. The basic safeguard of positive identification of all structures by careful dissection before division or ligation is the same in either case. Strict adherence to this rule should positively prevent dangerous errors.

Most of the difficulties center about the cystic artery. A well known but frequently ignored fact accounts for some of the sudden hemorrhage from the cystic artery. The cystic duct is convoluted and the cystic artery is not. If one is dissecting out the cystic duct first and he applies too much traction in order to straighten it, the cystic artery may be ruptured or, what is worse, pulled off from the

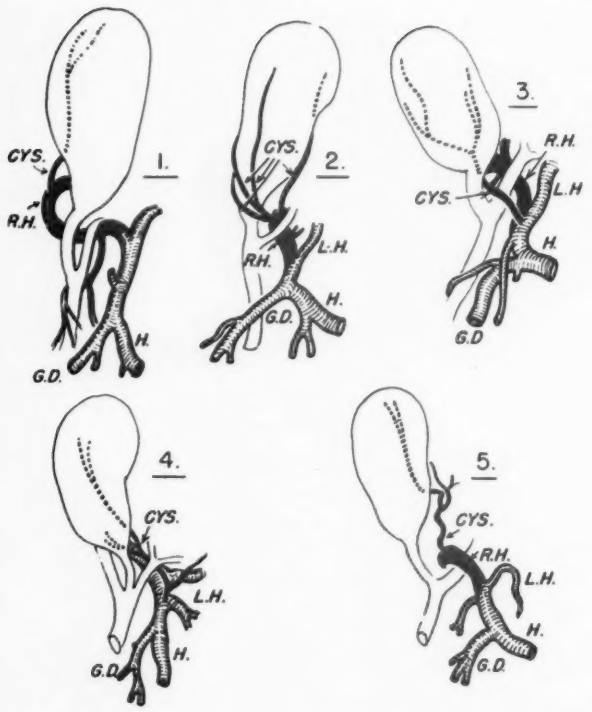

FIG. 1. Cystic artery type 1. (*1*) Gallbladder retracted to the left to demonstrate anatomy better. (*2*) Two cystic arteries, one arising to the right and one to the left of the hepatic duct, both from the right hepatic artery. (*3*) Dual cystic arteries fused distally, the larger from the left hepatic, the shorter from the right hepatic in the triangle of Calot. (*4*) Common type cystic artery with accessory right hepatic duct. (*5*) Cystic artery arises to right of common hepatic duct from the right hepatic artery, crossing anterior to common hepatic duct.

right hepatic artery, a formidable problem. This is the chief reason the cystic artery should be dealt with first if at all possible, and it is most of the time.

There is a great deal of anatomical variation in the cystic artery. At least twelve different sites of origin have been described. As Cole [*3*] has said, "It is impossible to set up a normal picture of the anatomy of the biliary tract in one's mind. All one can do is to set up a composite of the commoner types." It is important to remember that an artery which looks like a cystic artery and courses near and parallel with the cystic duct is not necessarily the cystic artery [*4*]. More often than not it is the right hepatic artery. I am sure that many of us, including myself, have been about to clamp such an artery thinking it was the cystic. The precaution of positive identification before ligation stimulates a further look and proper identification of the cystic artery. A helpful safeguard if there is some question is to look on the gall bladder itself. Here you will find the superficial cystic artery which can be followed back to remove all doubt.

Typically the cystic artery arises from the right hepatic artery to the right of the hepatic duct in Calot's triangle. The boundaries of this are inferolaterally the cystic duct, medially the hepatic duct and cephalad the liver. The right hepatic artery and the cystic artery are predominantly located in the upper part of the triangle, the right hepatic artery having crossed under or over the hepatic duct to reach the triangle. The course of the cystic artery in the triangle may be short or long depending on its site and mode of origin. On reaching the gallbladder it usually bifurcates into its characteristic superficial and deep branches, the cysticae gemellae which Vesalius spoke of in 1564. The superficial branch goes to the free peritoneal surface of the gallbladder. The deep branch courses behind the gallbladder to be distributed to its attached non-peritoneal surface and to the gallbladder bed.

In a series of 580 dissections of the cystic artery, Daseler and his associates [*5*] found that 405 (69 per cent) arose in Calot's triangle. The following variations were found in this study. They are presented in order of frequency with representative illustrations adapted from the aforementioned study.

The first type, comprising 58.6 per cent (Fig. 1), had the cystic artery arising as a branch of the right hepatic artery to the right of the hepatic duct in the angle formed by that structure and the cystic duct. This type can be further subdivided into (A), in which the right hepatic artery crosses posterior to the common duct and (B), in which it crosses anterior to the common duct.

In the second type, comprising 13.1 per cent (Fig. 2), the cystic artery arose from the proximal portion of the right hepatic artery before the latter had crossed from left to right, dorsal or ventral to the hepatic duct. The cystic artery then crossed the hepatic duct. The total incidence of the cystic artery crossing the hepatic ducts in this study was 21.2 per cent.

Found less frequently was the third type (Fig. 3), comprising 11.9 per cent, in which the cystic artery arose from an aberrant right hepatic artery derived from the superior mesenteric artery. In about one-fifth of this group a dual cystic arterial arrangement was found.

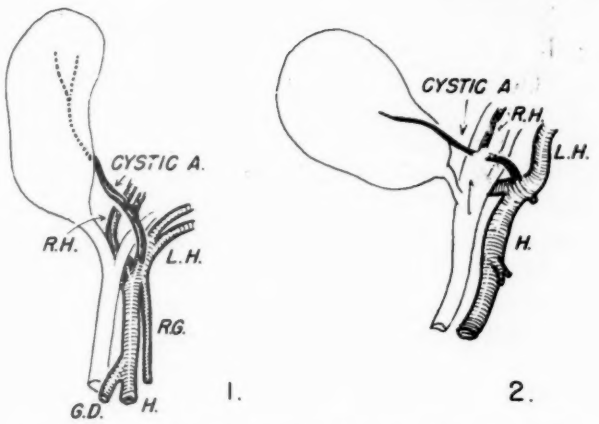

FIG. 2. Cystic artery type 2. (*1*) Cystic artery arises from proximal portion of right hepatic artery to the left of common hepatic duct, then crosses anteriorly. (*2*) Cystic artery anterior. Here cystic duct drains directly into right hepatic duct.

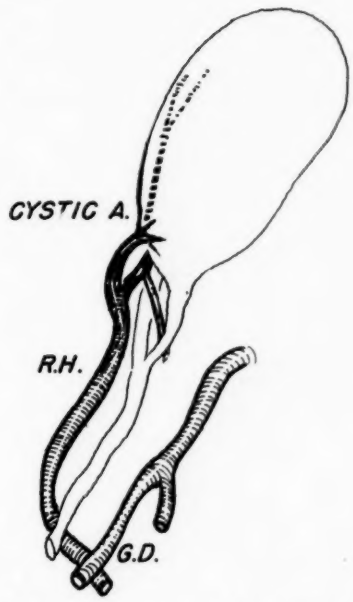

FIG. 3. Cystic artery type 3. Cystic artery arises from aberrant right hepatic artery derived from first portion of superior mesenteric artery. No common hepatic artery. Cystic artery runs to hepatic surface of gallbladder.

In the fourth most common type, comprising 6.2 per cent (Fig. 4), the cystic artery was derived from the left hepatic artery. Invariably in this group the cystic artery crossed anterior to the common hepatic duct. In 25 per cent of these cases there was an additional cystic artery present derived from another source than the left hepatic artery.

The fifth type in order of frequency, comprising 2.8 per cent (Fig. 5), demonstrated the cystic artery arising as a branch of the common hepatic artery. In 75 per cent of this group the cystic artery crossed anterior to the bile ducts.

There were seven other rarer types in which the cystic artery took origin from the gastroduodenal, accessory type right hepatic, the celiac axis, the superior mesenteric, the superior pancreaticoduodenal, the right gastroepiploic and the aorta. Doubling of the cystic artery was relatively common in this group, totalling 15 per cent over-all. It is obviously quite impossible and unnecessary to remember all the

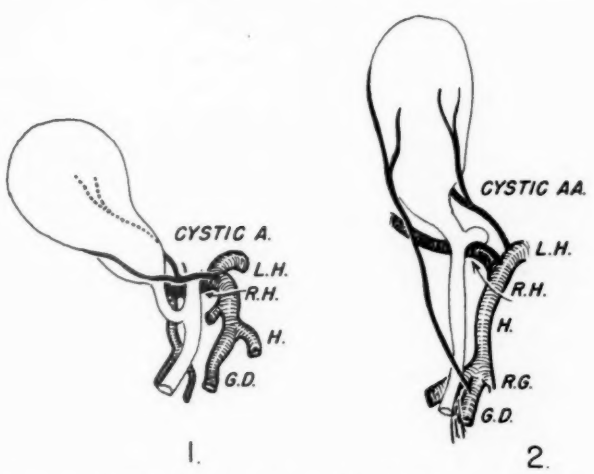

FIG. 4. Cystic artery type 4. (*1*) Cystic artery arises from left hepatic artery and crosses anterior to common duct. (*2*) Two cystic arteries, one from the gastroduodenal artery and one from the left hepatic artery, the latter crossing anterior to the common duct.

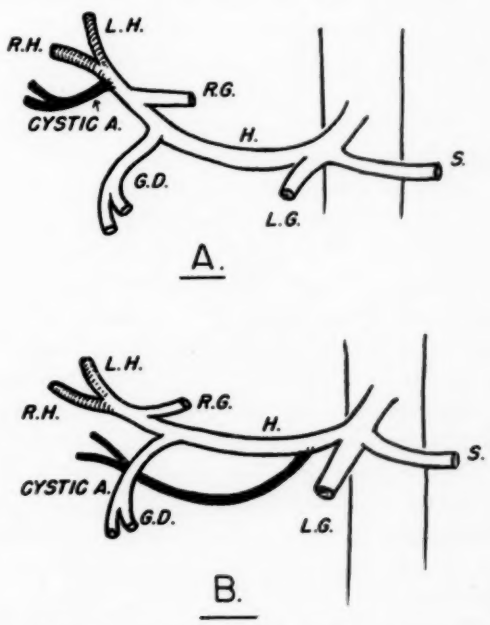

FIG. 5. Cystic artery type 5. A and B represent two examples of the origin of the cystic artery from the common hepatic artery.

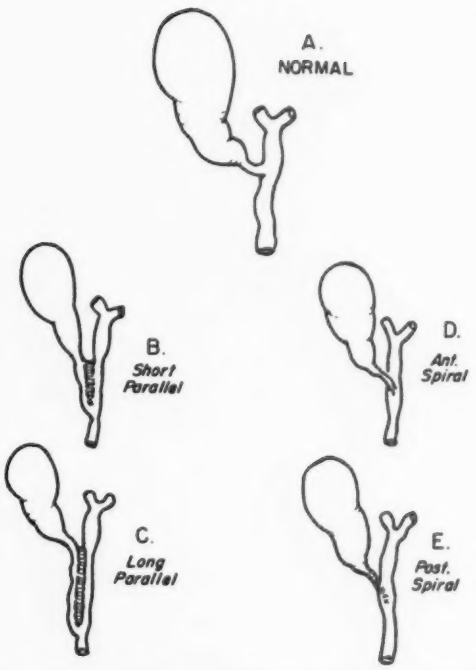

FIG. 6. Types of junction of the cystic with the common duct.

different types or to have them in mind at any one time. It is most important to be constantly and actively aware that many variations do occur, and on this basis to proceed with caution.

The handling of the cystic duct is usually less of a problem than the cystic artery. Ligation of the common duct at its junction with the cystic duct by traction on the cystic duct is inexcusable. Being aware that excessive length of the stump of the remaining cystic duct can lead to trouble and to subsequent surgery, it is important to ligate the cystic duct at the proper distance from the common duct. Rarely there may be an accessory hepatic duct (Fig. 1) or the cystic duct may empty into the right hepatic duct. (Fig. 2.) This is no problem as long as the junction of the cystic duct and the common or right hepatic duct is clearly demonstrated before the cystic duct is clamped or ligated. The duct must not be ligated so closely that postoperative edema will cause impingement on the common duct with potential partial obstruction and infection. A distance of from .5 to 1 cm. from the junction is usually sufficient but this may have to be modified if there is an unusually large diameter to the cystic duct.

In this connection one of the reasons for leaving too much cystic duct is the failure to know or realize that there are different types of junctions of the cystic with the hepatic duct. As pointed out in the work of Johnston and Anson [6], there are five main types shown here. (Fig. 6.) Obviously it is in the long parallel where a small stone may be left, and in the posterior spiral types where too much cystic duct may be left because of inaccurate dissection. Again the safeguard of positive identification before ligation or clamping, in this instance the exact location of the junction of the ducts, will prevent both immediate and remote difficulty.

While on the subject of protection of the common duct, it must be emphasized that great care must be taken in dissecting out the redundant ampulla of the gallbladder, the so-called Hartmann's pouch, when it occurs. Occasionally this may lie under the common duct and must be dissected out very carefully. This is particularly so if there is acute or recent inflammation present, in which case the ampulla of the gallbladder may be adherent to the duct.

When the cystic artery and duct have been ligated (I use two No. 2-0 chromic catgut ties on each structure), peritoneal flaps are raised on either side of the gallbladder and it is removed between these flaps. This, of course, may be impossible to do when an acute condition of the gallbladder exists but with this exception it can almost always be done and with a good reason. These flaps are sewed together with a lock stitch which controls bleeding, and with the gallbladder bed covered with peritoneum there is less chance for adhesive complications. These flaps should be carefully inspected before and after suturing. Occasionally a brisk bleeder may be encountered requiring clamping and ligation. I have a very vivid memory of having to reoperate upon a medical student, on the evening following an uneventful cholecystectomy, to control an active bleeder in the lower peritoneal flap which had been sewed to the upper with a running stitch at the first operation.

Because of the almost constant presence of small accessory bile ducts which may pour out copious amounts of bile postoperatively, I believe a drain is always indicated. I have been inclined to bring this out through a stab wound just lateral to the incision as a precaution against possible wound infection.

There is then, as I said at the beginning, nothing new to offer in the technic of cholecystectomy. One must not allow his technic to become hasty, careless or sloppy. A series of so-called easy operations upon the gallbladder may lull one into a false sense of security about his ability and skill. To repeat Dr. Lahey's admonition, this is a dangerous operation. With carefully controlled dissection it should be 100 per cent safe as far as hemorrhage and the integrity of the bile ducts are concerned. As with liberty, the price of safe cholecystectomy is constant vigilance.

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Acute Cholecystitis

JOHN J. BYRNE, M.D.,* *Boston, Massachusetts*

THE management of acute cholecystitis is an often debated problem despite the vast amount of study which it has engendered. Most textbooks of surgery mention two courses of action: a conservative, watchful-waiting approach which is stirred from its complacency only by the clinical evidence of impending gangrene or perforation, and an aggressive early-operation discipline. Since each hospital population differs with regard to age and physical condition, it should adopt the method dictated by its own experience. In order to do this, 134 consecutive cases of acute cholecystitis seen prior to 1958 were carefully reviewed. The results indicate that the best system is operation as early as possible but commensurate with the time needed to make an accurate diagnosis and to place the patient in an optimal condition to withstand the operation.

PATHOLOGY

Seventy-five pathological specimens were measured and examined microscopically, and form the basis for the material in this chapter.

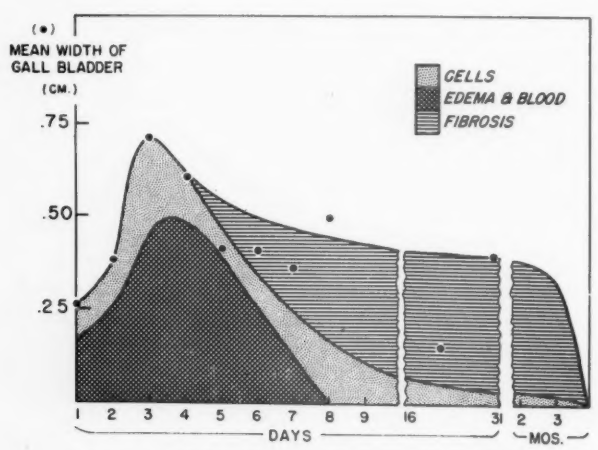

FIG. 1. Mean width and general composition of gallbladder walls at various intervals during acute cholecystitis.

The most measurable change in the process of acute cholecystitis is the increase in the *thickness* of the gallbladder wall. As can be seen (Fig. 1), there is a marked increase during the first few days, reaching a peak on the third or fourth day, after which it slowly diminishes over the next few weeks or months. What produces this increase in width? It consists of cells, edema, blood and fibrosis, but in different proportions at various stages of the disease.

On the first day there is mild hemorrhage and congestion with moderate edema. (Fig. 2.) These changes increase during the next few days, reaching their peak on the third or fourth day (Fig. 3), after which they diminish and disappear by the sixth or seventh day.

The cellular infiltrate is chronic in most cases (89 per cent), but when infection supervenes it is acute (11 per cent).

As the edematous, hemorrhagic reaction subsides, healing takes place by fibrosis. Young fibrous tissue is pronounced by the ninth and tenth days. (Figs. 4 and 5.) The fibrous tissue then begins to mature and shrink (Figs. 6 and 7) and perhaps resolve. This process may require two (Fig. 8) or three months.

From the point of view of ease of operating, dissection is simpler with the edematous or young fibrous reaction than with the mature fibrous reaction. This would suggest that in such cases operation should be performed during the first ten to twelve days. One should then wait three to four months before operating unless there are other indications for surgery.

This pathological sequence may be interrupted at any time by *gangrene* or *infection*. As one would expect from the review of the pathology, the gangrene and its complications are most apt to happen before the onset of marked fibrosis whereas infection may occur at any time

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FIG. 2. Gallbladder wall on first day of acute process showing edema, hemorrhage and congestion.

FIG. 3. Gallbladder wall on fourth day of acute cholecystitis showing maximum edema and congestion and cellular reaction.

during the sequence. Gangrene with free or local perforation occurs during the first eight days, with a peak on the third day. (Fig. 9.) Infection as manifested by empyema or perforation with localized abscess is first seen on the third day and appears more frequently during the next seven days but is observed even up to thirty-one days following onset. This would suggest that if gallbladders are removed early, many of these complications would be avoided.

PATHOGENESIS

The previously described pathologic process is usually produced by obstruction of the gallbladder by a stone impacted in the cystic duct. If the obstruction is relieved, the process re-

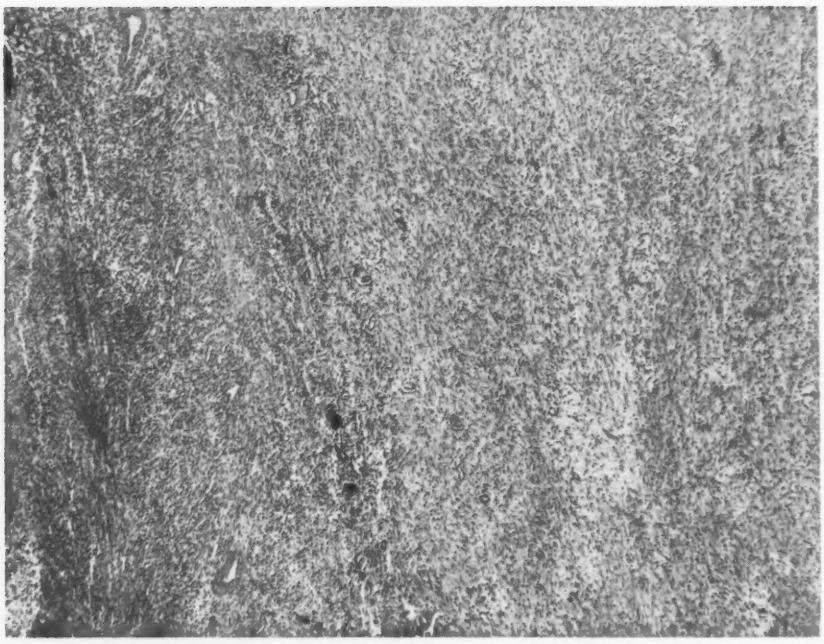

FIG. 4. Acute cholecystitis, ninth day after onset; abundant fibrous tissue can be seen.

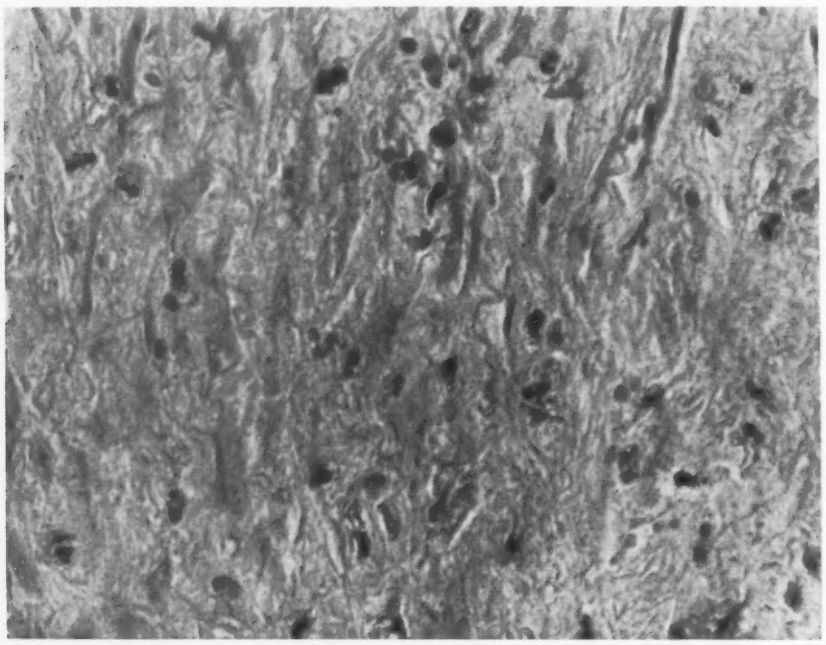

FIG. 5. High power view of Figure 4; note the young fibrous tissue.

solves. If the obstruction is unrelieved, several possibilities occur. The increasing distention of the obstructed gallbladder results in ischemic changes in the wall at points farthest from the blood supply (*gangrene*). The mucosa is affected first and the gangrene may then spread to involve the entire wall.

Perforation may occur into a localized pericholecystic area or into the general peritoneal cavity. Occasionally it may penetrate an adjacent viscus and produce a biliary fistula [*1*]. Such perforation may rarely occur at the site of the impacted stone in the cystic duct or at the site of a carcinoma which has developed in the calculous gallbladder. Massive intraperitoneal hemorrhage may be associated with perforation and thirteen cases have been reported with a mortality of 46 per cent [*2*].

One case appeared in this series with a massive hematoperitoneum produced by perforated acute cholecystitis, with survival.

If the process terminates before perforation occurs, the gallbladder will heal by fibrosis over the course of many months.

The gallbladder content is bile in most cases unless the bladder was empty at the time of obstruction, in which case it will become distended with mucus (*hydrops*). (Fig. 10.)

A very unusual recovery following free perforation has been reported by Moragues and Simon [3] with the finding of numerous gallstones throughout the abdomen in a patient with a previous "silent" clinical history.

Although the cause of obstruction is usually

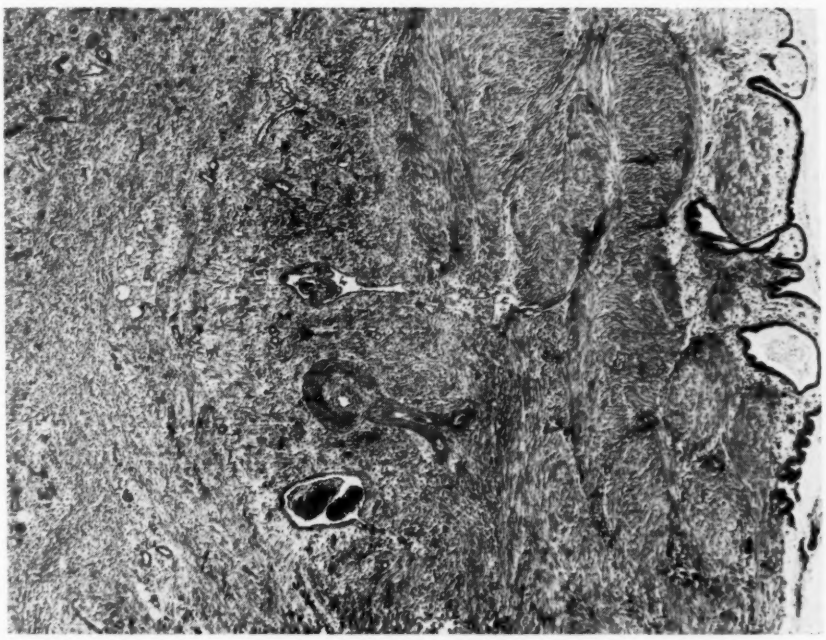

FIG. 6. Acute cholecystitis, twentieth day after onset, with marked fibrous tissue response.

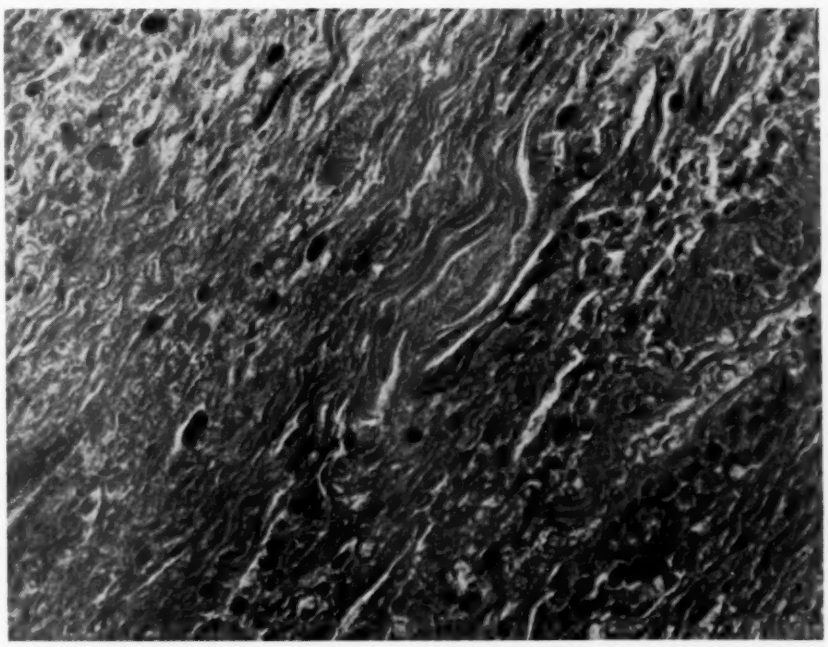

FIG. 7. High power view of Figure 6; note the more mature fibrous tissue.

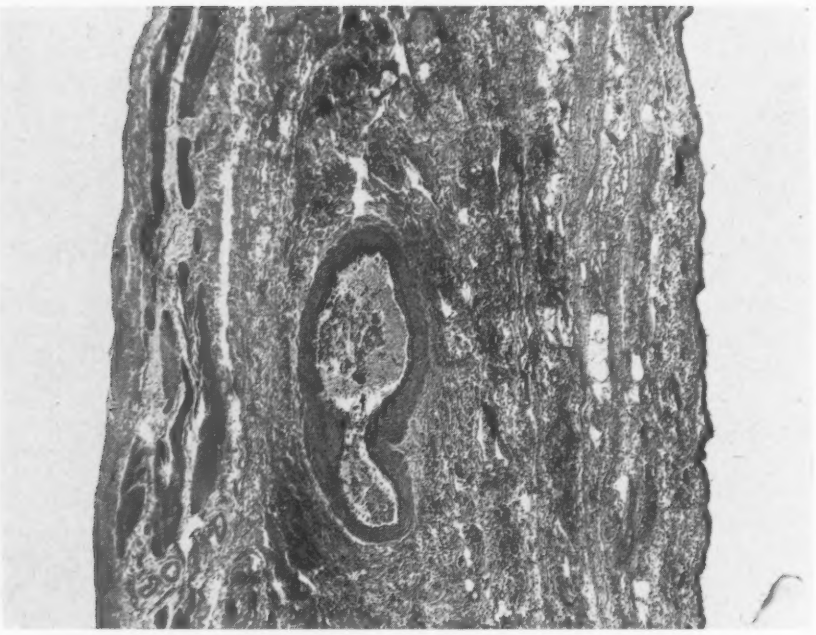

FIG. 8. Acute cholecystitis sixty days after onset; marked fibrosis.

a stone in the cystic duct, rarely there may be other causes, such as a stricture or kinking of the cystic duct, intussusception of a polyp [4], torsion of the gallbladder or pressure of an overlying lymph node on the cystic duct. The average incidence of stone is over 90 per cent in most series [5–7], and in this series it was 92 per cent. In the remaining ten cases the obstruction was due to carcinoma of the pancreas and torsion of the gallbladder in individual cases. Thus only eight cases appeared to have no obstructing cause. However, since tiny stones are easily overlooked in long cystic ducts, I believe that they may have been overlooked in these cases.

In addition to obstruction there are other factors of varying importance such as inflammation and vascular occlusion. The inflammation may be produced by either infection or chemical irritation.

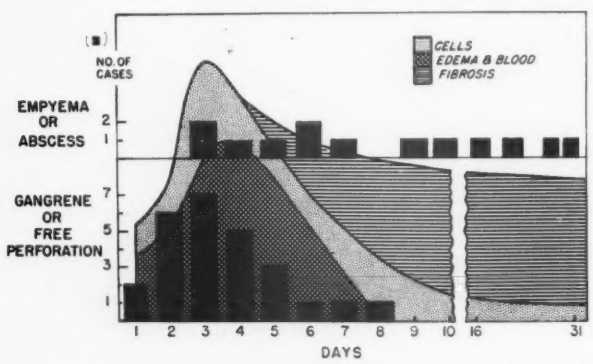

FIG. 9. Occurrence of gangrene or perforation and empyema or abscess with relation to duration of disease and composition of the gallbladder wall.

The infection is usually a secondary phenomenon with bacteria invading the edematous gallbladder either by blood stream, lymphatics or biliary tree. Bacteria are found in the bile in 29 per cent of the cases and in the gallbladder wall in 45 per cent [8]. The usual organisms found in acute cholecystitis are Escherichia coli, Bacterium aerogenes, and non-hemolytic streptococcus and rarely Bacillus proteus, staphylococcus and clostridia. Klebsiella may be a secondary invader misdiagnosed as Esch. coli unless a capsule stain is done [9]. Baehr et al. [10] found among 198 such cases that 30 per cent of the deaths were due to cholangitis, pyelophlebitis and liver abscess.

The gallbladder may become filled with pus (*empyema*) which may rarely perforate into surrounding tissues (*pericholecystic abscess*) and very rarely into the free peritoneal cavity.

If the secondary invader is a gas-producing organism, a variant of acute cholecystitis may occur known as cholecystitis emphysematosa or *pneumocholecystitis*. Diabetes is a predisposing factor to this disease. The usual organisms are Clostridium welchii, Esch. coli, streptococci and staphylococci. Gas may be seen in the gallbladder and produce a fluid level, or may extend into the surrounding tissue. Often a halo of decreased density is seen around the

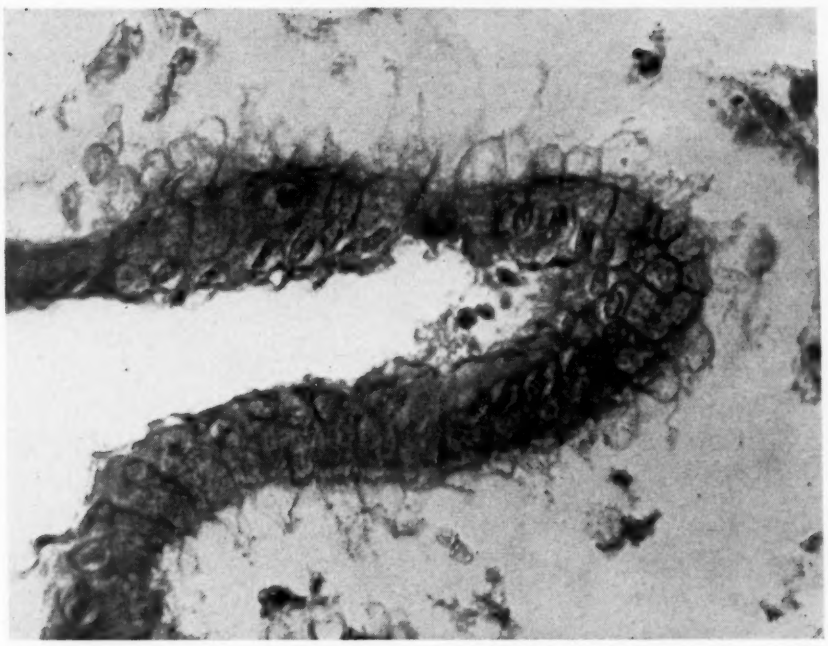

FIG. 10. High power view of hydrops of gallbladder with much mucus being produced by the mucosal cells.

gallbladder shadow. This has been the object of much controversy, with many observers believing it represents air-filled Rokitansky-Aschoff sinuses. However, experimental studies have shown it represents perimuscular air appearing first near the cystic duct and spreading to the fundus [*11*]. The air may be confused with a biliary fistula or lipomatosis of the gallbladder.

Occasionally the infection may be primary, particularly in children; but with the development of antibiotics this is on the wane [*12*]. However, there are still rare case reports of such with the organism involved being Eberthella typhosa [*13*], Salmonella oranienburg, and even ascaris [*14*].

A rare complication is colon bacillus septicemia which may begin abruptly in patients who are otherwise in good health [*15*]. The initial attack of acute cholecystitis occurs which may be soon followed by chills, fever and other signs of toxemic prostration with or without jaundice. Blood cultures are positive for Bacillus coli. We have had three experiences with such complications. One patient died following operation after a prolonged period of conservative therapy, and one died on the fifth day of disease without operation. It would seem that the prevention of this complication would be another reason for early surgery in acute cholecystitis.

Chemical irritation by pancreatic juice or bile may play a role in the pathogenesis. Concentrated bile has been substantiated experimentally as being an important secondary agent in this process [*16*]. However, the pathology of the gallbladder with hydrops is not unlike that filled with bile. (Fig. 11.) It does not appear evident that the chemical nature of bile *per se* plays much of a role in the pathogenesis.

Vascular factors are also of secondary importance. Edema at the cystic duct may produce obstruction of the cystic vein and lymphatics, spasm of the cystic artery or thrombosis of the cystic artery. However, the collateral circulation from the liver should overcome these factors if the arteries of the gallbladder wall are not obstructed by the distention. This would account for the low incidence of perforation in acute cholecystitis which ranges up to 10 per cent in large series [*5–7*]. The fact that aged people and those with associated vascular disease have more perforation or gangrene is good evidence that vascular factors play a role in the pathogenesis.

To summarize then, the most important factor in the production of acute cholecystitis is obstruction of the cystic duct. This may be augmented by infection which may increase the distending pressure or weaken the gallbladder wall. Vascular diseases may further enhance the tension gangrene which may de-

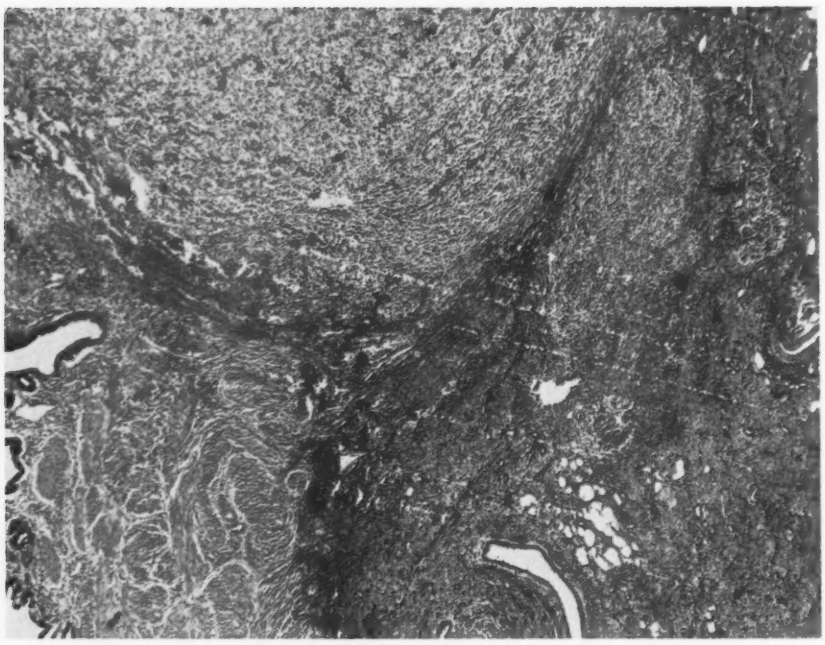

FIG. 11. Hydrops of gallbladder six days after onset; lumen filled with white bile. No pathological difference from ordinary acute cholecystitis.

velop. The sooner the obstruction is relieved, the sooner the patient will be relieved.

EPIDEMIOLOGY

The sex and age ratios of this population are similar to those of other studies of acute cholecystitis. Eighty-two patients (62 per cent) were women, twice as many as men. This ratio was maintained in the various age groups. (Fig. 12.)

The age distribution (Fig. 13) may be summarized briefly: The youngest patient was twenty-four years of age, the oldest ninety-one, and the mean age about fifty-two. Thirty-nine per cent of the patients were over sixty, and this group accounted for 71 per cent of the deaths and 64 per cent of the gangrenous or perforated cases.

As one would expect, there were many associated cardiovascular diseases in this elderly population. (Table 1.) Thirty-six cases were observed and twenty-two had a complication of gallbladder disease such as perforation, gangrene or empyema. In other words, 61 per cent of the complications appeared in people with obvious associated vascular disease (25 per cent of this series). Fifteen of the sixteen deaths (94 per cent) also occurred in this group.

The associated diseases demand a little more

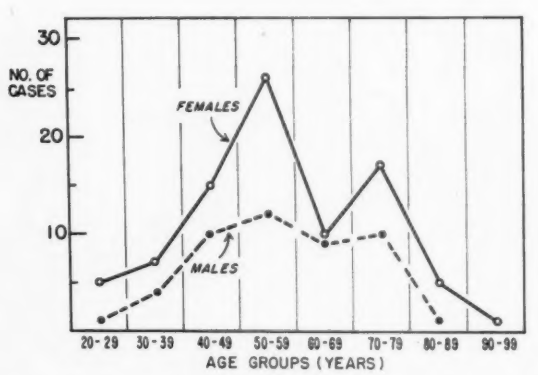

FIG. 12. Age and sex frequency distribution of acute cholecystitis.

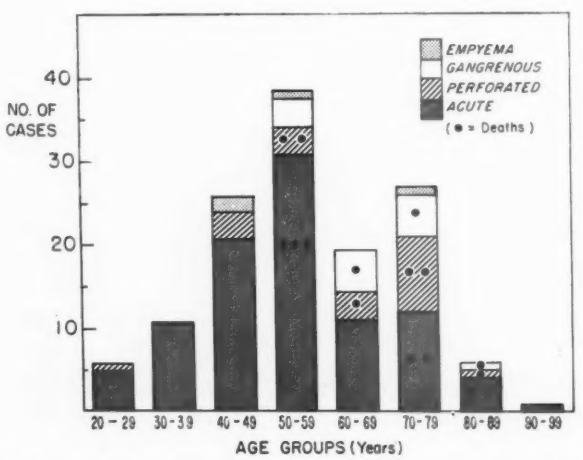

FIG. 13. Age distribution of patients with various types of acute cholecystitis.

TABLE I

ASSOCIATED DISEASES WITH DEATHS AND GALLBLADDER COMPLICATIONS IN THIS SERIES OF 134 CASES OF ACUTE CHOLECYSTITIS

	No. of Cases	No. of Deaths	Complications		
			Perforations	Gangrene	Empyema
Heart disease:					
Arteriosclerosis	18	9	6	3	0
Hypertension	3	0	0	1	0
Rheumatic fever	1	1	0	0	0
Diabetes mellitus	6	3	4	0	1
Leukemia	3	1	2	1	0
Glomerulonephritis	2	0	0	2	0
Pernicious anemia	1	0	0	0	1
Purpura	1	0	1	0	0
Emphysema and asthma	1	1	0	0	0
Total	36	15	13	7	2

scrutiny. Eighteen patients had advanced arteriosclerotic heart disease that accounted for nine deaths and nine complications of gallbladder disease (three pericholecystic abscesses, two free gangrenous perforations, one free localized perforation and three cases of gangrene). In six diabetic patients there were five complications of gallbladder disease (two free generalized perforations, two localized pericholecystic abscesses and one empyema), with three deaths. Three patients with leukemia had complications of gallbladder disease (two free localized perforations and one gangrene perforation), with one death.

The occurrence of acute cholecystitis in association with the treatment of unrelated diseases, especially their surgical treatment, has been well stressed [*17,18*]. Patients with gallstones who are hospitalized for unrelated disease are subject to many factors which could precipitate an attack: fasting diet, sphincter-contracting narcotics, dehydration, supine position, anesthesia, infection, fright, etc. In this series acute cholecystitis developed during the treatment for pernicious anemia, leukemia, diarrhea and pulmonary emphysema and asthma. It followed surgery in two cases, one a fulguration of a tumor of the bladder, and the other incision and drainage of an abscess in a diabetic patient.

In the patient with the tumor of the bladder purpura developed which was treated with cortisone. On cessation of cortisone, the acute cholecystitis developed. The cortisone may not only have masked the onset of the disease, but also it may have fostered the infectious element, since a large pericholecystic abscess developed in a forty-eight year old woman. The drug may also have prevented the normal fibrotic response.

SIGNS AND SYMPTOMS

Do any of the presenting symptoms or signs warn of a complication of gallbladder disease? If they did, a watchful conservative approach might be made safer.

The majority of patients presented themselves because of pain in the right upper quadrant (73 per cent) or in the upper part of the abdomen (15 per cent). (Table II.) Five patients had pain in the right lower quadrant of the abdomen, and three had either gangrene or perforation. Similarly, five patients suffered from generalized abdominal pain, three having perforation or empyema. These peculiar sites for the pain were explained in some of the cases by leakage of bile down the right gutter. Five patients had no abdominal pain, two had a perforated gallbladder and one had empyema. There was one patient who complained of pain in the anterior chest. Radiation of the pain occurred in fifty-five patients (41 per cent) and was equally divided to the back (twenty-seven patients) or right scapular area (twenty-six). In one, the pain referred to the left scapula and in another to the right lower portion of the abdomen. No prognostic significance was attached to the radiation.

TABLE II

SYMPTOMS OF ACUTE CHOLECYSTITIS TOGETHER WITH PERCENTAGE OF TOTAL COMPLICATIONS FOUND WITH EACH SYMPTOM

	No. of Cases	Percentage of Cases	Percentage of Complications
Location of pain:			
Right upper abdominal quadrant	98	73.0	70.0
Upper abdominal quadrant	20	15.0	8.3
Right lower abdominal quadrant	5	3.7	8.3
Generalized	5	3.7	8.3
None	5	3.7	5.1
Anterior chest	1		
Radiation of pain:			
Back	27	20.0	17.0
Right scapula	26	19.0	8.4
Left scapula	1		
Right lower quadrant of abdomen	1		
Vomiting	83	62.0	58.0
Chills	7	5.0	2 deaths

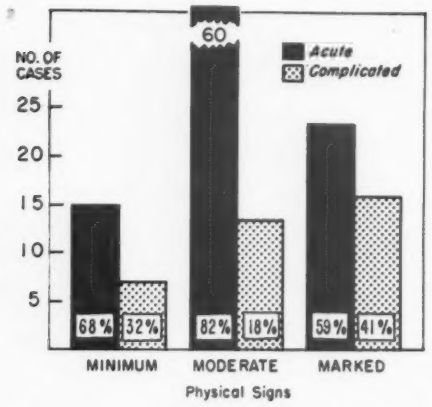

FIG. 14. Correlation of severity of physical signs with the condition of the gallbladder.

Vomiting appeared in eighty-three (62 per cent) of the cases. It bore little correlation with the severity of the case since only 54 per cent of the complications—such as perforation, gangrene or empyema—appeared in this group.

Seven patients exhibited chills on admission. In three cases this represented cholangitis; one patient subsequently died of B. coli septicemia. Another patient died suddenly immediately postoperatively and may have represented a case of septic shock. Thus this symptom may have a slightly ominous significance since 12 per cent of the deaths occurred in this small (5 per cent) group.

Tenderness (Table III) was elicited in varying degrees in every case except three. In 115 patients (86 per cent) it was found in the right upper abdominal quadrant, and in four patients in the epigastrium. Occasionally (eleven cases) tenderness was found over the right side of the abdomen, the entire abdomen or in the right lower quadrant. As one would expect, this indicates spread of peritoneal inflammation, and perforation and gangrene were found in seven (63 per cent) of these instances.

Rebound tenderness was found in twenty-four cases (18 per cent). This finding should mean more advanced peritoneal irritation but actually only 16 per cent (six) of the complications appeared in this group.

Spasm was felt in seventy-seven cases (57 per cent) but carried no special warning, since only 50 per cent of the complications of gallbladder disease were found here. In five of the cases, however, there was generalized spasm and four of these cases were perforated or gangrenous.

A mass was found in sixty-nine cases (51 per cent), but contrary to many other studies it carried no prognostic implication since 53 per cent of the complications occurred here.

Of interest in this regard is Case 23, a sixty-six year old white woman who was examined in her doctor's office seven days following the onset of pain in the right upper quadrant of the abdomen. A mass was palpated in the right upper quadrant, but during palpation the mass disappeared associated with sudden generalized abdominal pain which went on to severe tenderness and a shock-like state. On her arrival at the Accident Floor the patient's temperature was 103°F., the pulse 100 and the white blood count 11,000 per cu. mm. The patient had had arteriosclerotic heart disease. She was immediately taken to the operating room and a gangrenous gallbladder was found with a perforation near its base. Although the mass itself may have no prognostic implication, the sudden disappearance of a mass during examination is a more serious problem.

Jaundice was present in eleven cases, which will be discussed subsequently.

It is thus seen that the usual signs afford little or no warning of the complications of gallbladder disease. The severity of the signs were a little more helpful. (Fig. 14.) Thus 41 per cent of these cases with marked signs had complications, as compared to 18 per cent of those with moderate signs. However, 32 per cent of those with minimal signs had complications.

Thus these figures bear out our impression and confirm those of other surgeons that there is a very poor correlation between signs and symptoms and the state of an acutely diseased

TABLE III

SIGNS OF ACUTE CHOLECYSTITIS AND PERCENTAGE OF COMPLICATIONS FOUND WITH EACH

	No. of Cases	Percentage of Cases	Percentage of Complications
Tenderness:			
Right upper abdominal quadrant	115	86.0	81.0
Epigastrium	4	3.0	0
Right side of abdomen	2	1.0	5.0
Generalized	6	4.0	11.0
Right lower abdominal quadrant	3	2.0	3.0
Rebound tenderness	24	18.0	16.0
Spasm:			
Right lower abdominal quadrant	77	57.0	50.0
Generalized	5	3.0	11.0
Mass	69	51.0	53.0
Jaundice	11	8.0	8.5

TABLE IV
CORRELATION OF WHITE CELL COUNT WITH PERCENTAGE OF COMPLICATIONS OF GALLBLADDER DISEASE

White Blood Count (in thousands per cu. mm.)	No. of Cases	No. of Complications	Percentage of Complications
Over 35	4	2	50.0
30–34.9	5	2	40.0
25–29.9	6	2	33.0
20–24.9	15	4	26.0
15–19.9	29	10	34.0
10–14.9	52	13	25.0
5– 9.9	22	2	9.0
0– 4.9	1	1	100.0
Total	134	36	26.8

gallbladder. Careful waiting and observation is usually careless waiting and blind guessing.

LABORATORY AIDS

Do any of the laboratory procedures aid in differentiating complicated from uncomplicated gallbladder disease?

The white blood count has been a time-honored guide and in a broad sense is of some help. (Table IV.) As can be seen, there is a general correlation between the white blood count and the incidence of complications.

If an artificial index is made (*the inflammatory index*) which includes white blood count, pulse and temperature (Table V) and is calculated for each case, one finds that in general a high inflammatory index means a complication. (Fig. 15.) However, we still find complications

TABLE V
INFLAMMATORY INDEX*

White Blood Count (in thousands per cu. mm.)	Pulse Rate	Temperature (°F.)
Over 30..... 3	Over 120..... 3	Over 102..... 3
20–29.9..... 2	100–119..... 2	100–101.9..... 2
10–19.9..... 1	80–99..... 1	98.6–99.9..... 1
0–9.9..... 0	Under 79..... 0	Normal..... 0

* Inflammatory index is the sum of indices assigned to various elevations of white blood count, pulse and temperature. Example: Temperature 101°F., pulse 96 and white blood count 21,000 per cu. mm. Inflammatory index = 5.

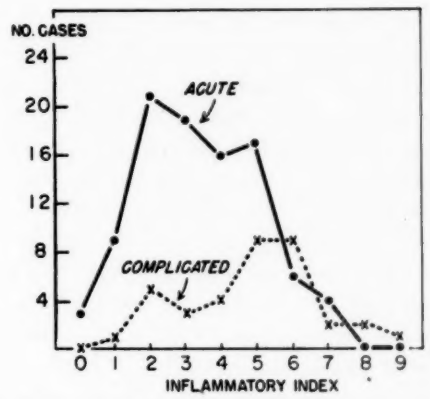

FIG. 15. Frequency distribution of inflammatory index for acute and complicated gallbladder disease.

TABLE VI
INDICES FOR ASSOCIATED DISEASES AND AGE

Age		Associated Vascular Diseases	
Under 60.....	0	Diabetes.....	3
60–69.....	1	Arteriosclerotic heart disease	3
70–79.....	2	Leukemia.....	3
Over 80.....	3	Purpura.....	3

occurring in persons with a low inflammatory index; and in searching around for an aid to this, if we remember that most of these complications occur in the aged and in those with associated vascular disease, we could add these factors to the inflammatory index. (Table VI.) When these revised indices are correlated with the presence or absence of complications, we find a better correlation. (Fig. 16.)

In other words an acutely diseased gallbladder in an elderly patient with associated

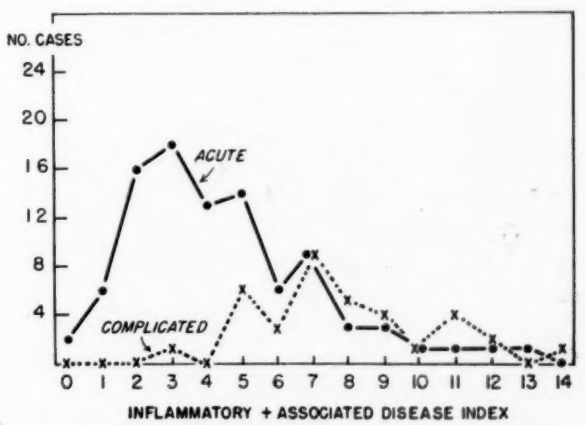

FIG. 16. Frequency distribution of inflammatory associated disease index for acute and complicated gallbladder disease.

vascular disease is more apt to be perforated or gangrenous.

X-rays were taken in forty-eight cases and usually confirmed the diagnosis of a non-functioning gallbladder. Twenty-eight Graham-Cole series were taken which showed no or poor visualization. No untoward events followed these. In eight cases stones were seen on the flat plate. Besides diagnosis x-ray examination may have prognostic significance. In nine cases an elevated right diaphragm was demonstrated and six of these were associated with gangrene or perforation. We should thus pay more attention to this in our diagnostic workup. The sign must be due to immobilization of the muscles surrounding the right upper abdominal quadrant. Lumbar scoliosis with the concavity to the right also may be seen. Obvious ileus usually means perforation.

DIFFERENTIAL DIAGNOSIS

Although the diagnosis of acute cholecystitis is quite obvious in most cases, there are many diseases which can mimic it. Many of these are surgical and hence an error is not so serious. In four or five cases, however, surgery is definitely contraindicated and may cause death. Therefore every case demands study. Right upper quadrant abdominal pain, tenderness and spasm do not always mean acute cholecystitis.

There are three categories into which these diseases can be placed: contained, referred or spilled.

The organs contained in the right upper quadrant include the skin, fat, muscles, nerves, peritoneum of the parietes and diaphragm, in addition to the gallbladder, liver, transverse colon, duodenum, head of the pancreas and kidney. (Fig. 17.) The list of diseases of these would be too long to enumerate. We were fooled during this series by the following diseases in this category: pancreatitis (five), tuberculosis of the diaphragmatic peritoneum, hepatitis, amebiasis of the colon and liver, and pyelonephritis. In addition there were three cases of carcinoma of the gallbladder masquerading as acute cholecystitis. The serious import of some of these operations may be gleaned from the fact that those patients with hepatitis, diaphragmatic tuberculosis and one of the five with pancreatitis died. In a special study at this hospital, the operative mortality rate for cases of hepatitis was 33 per cent.

Many diseases produce referred pain in the right upper abdominal quadrant. (Fig. 18.) We were fooled by none of these, but the warning about coronary disease and pneumonia

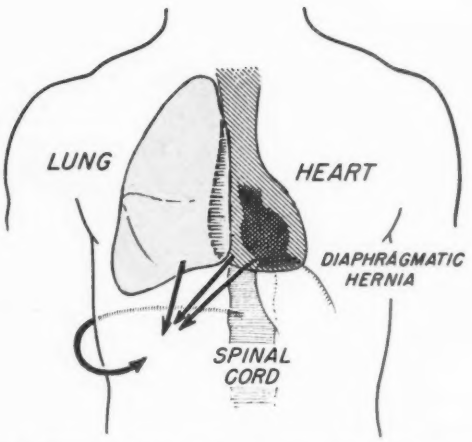

FIG. 18. Organs which may *refer* pain to the right upper abdominal quadrant.

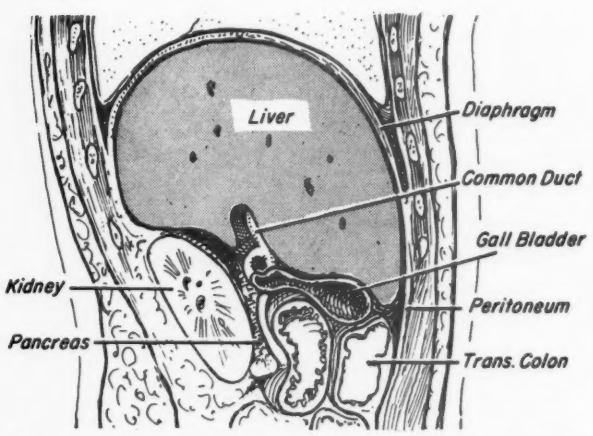

FIG. 17. Organs *contained* in the right upper abdominal quadrant.

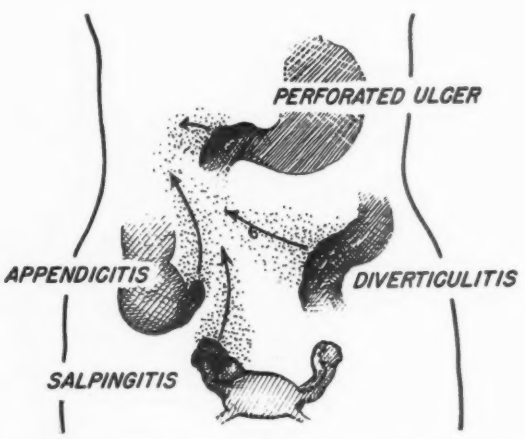

FIG. 19. Diseases which may spill fluid or pus into the right upper abdominal quadrant.

must always be emphasized, since operations on these people may also result in death.

Many diseases produce fluid or pus which may spill into the right upper quadrant. (Fig. 19.) Our obvious problems here are perforated ulcers and appendicitis. Since these are surgical problems, operations do not harm the patient but only the surgeon's pride in his diagnostic acumen. One patient with the Fitz-Hugh Curtis syndrome (pus under the diaphragm from salpingitis) was mistakenly operated upon without untoward consequences.

Thus *sufficient time* must be taken to rule out many of these diseases, particularly heart disease, pneumonia, hepatitis, pancreatitis and pyelonephritis.

CHOICE OF OPERATION

The preferred operation is cholecystectomy; but whenever the patient's general condition is poor or when the pathological findings are too severe, cholecystostomy is performed. Eighty patients underwent cholecystectomy, with four deaths (5 per cent mortality), whereas thirty-three underwent cholecystostomy, with nine deaths (27 per cent mortality). As one would expect, this latter group of patients was older (70 per cent over sixty years of age). The pathologic condition was more complicated (57 per cent were either perforated, gangrenous or empyemic) and there were more associated vascular diseases (37 per cent). (Table VII.)

TABLE VII

TYPE OF OPERATION FOR ACUTE CHOLECYSTITIS WITH RELATION TO AGE OF PATIENT, COMPLICATIONS, ASSOCIATED DISEASE AND MORTALITY

	Cholecystostomy		Choledochostomy		Cholecystectomy	
	No.	%	No.	%	No.	%
Over 60 yr. of age	23	70	7	35	23	29
Complications	19	57	1	5	19	24
Associated diseases	12	37	3	15	19	24
Total cases	33	..	20	..	80	..
Deaths	9	..	3	..	4	..
Mortality	..	27	..	15	..	5

One of the more controversial aspects of treatment of this disease is, When should one explore the common duct? These patients are usually poor risks and any prolongation of the operating time may be disastrous. The obstructing cystic duct is usually small and will not permit other than tiny stones to pass through it. If these stones pass through the cystic duct, why can they not pass through the common duct? The inflammation of the acute process may produce an obstructive jaundice which will subside when the obstructed gallbladder is treated. Ten jaundiced patients in this series did not have exploration of the common duct and only one had subsequent common duct stones. Twelve jaundiced patients had exploration of the common duct and stones were found in only six. Thus fifteen of twenty-two patients had obstructive jaundice produced by inflammation and not by stones.

How often are common duct stones seen in acute cholecystitis? Seven of the jaundiced patients had stones. Two of the non-jaundiced patients undergoing choledochostomy had them, and two other patients subsequently were found to have common duct stones. Thus only eleven patients (8.2 per cent) had stones.

Therefore, when one considers that the jaundice is usually caused by edema and only infrequently by stones, one must have very definite indications before exploring the common duct which will prolong the operating time in this precarious group of patients.

The severity of the jaundice might help. Sixteen patients had minimal to mild obstructive jaundice and only three had stones; whereas of six moderately to severely jaundiced patients, four had stones.

The palpation of a stone or evidence of chronic pancreatitis would probably demand exploration of the common duct, and a dilated or thickened common duct with multiple tiny stones in the gallbladder would suggest exploration of the common duct.

This point is emphasized since four of the common ducts explored for no particular reason produced no stones and two of these patients died.

The general condition of the patient must never be neglected, because biliary surgery can be staged. A cholecystostomy with removal of all the stones from the gallbladder may drain the biliary tree sufficiently to permit a later more definitive procedure.

Our statistics on the common duct are interesting. Seventeen patients had no associated vascular disease and there were no deaths. Three patients had such vascular disease and died: two in their eighties had arteriosclerotic heart disease and one age fifty-four had rheu-

matic heart disease. In two of the latter cases no stones were found on exploration.

Thus in acute cholecystitis with associated vascular disease one must be as certain of finding stones as possible before the common duct is explored, and even then a lesser procedure may accomplish the same purpose.

MORTALITY

Seventeen deaths occurred in this group of 134 patients. One patient had a carcinoma of the pancreas with associated acute cholecystitis, and I will not include this since it represents death from carcinoma of the pancreas and not from acute cholecystitis. Thus we had sixteen deaths in 133 patients (12 per cent). (Table VIII.)

Fifteen deaths (94 per cent) were due to associated diseases. Nine patients had arteriosclerotic heart disease (average age seventy-two); three had diabetes with perforation; one each had emphysema, rheumatic heart disease and leukemia.

Were any of these deaths due to precipitous surgery? Six occurred in patients operated upon on the day of admission. Three had gangrene or perforation which demanded surgery. Three, however, underwent surgery of the common duct. In two, no stones were found and the reason for the exploration was not evident. One patient was in shock and biliary peritonitis was suspected. On exploration, stones were felt in the common duct. Perhaps in this case cholecystostomy alone would have drained the biliary tree. Since these three patients had associated diseases, perhaps more time could have been taken to prepare them for surgery; certainly a better choice of operation may have helped.

TABLE VIII

MORTALITY FROM ACUTE CHOLECYSTITIS WITH RELATION TO CONDITION OF GALLBLADDER

	No. of Cases	No. of Deaths	Mortality Percentage
Perforations	20	6	30.0
Local abscess	9	2	22.0
Free, generalized	5	4	80.0
Free, localized	6	0	0
Gangrene	15	3	20.0
Empyema	4	0	0
Acute	94	7	7.4
Total	133	16	12.0

Were any of the other deaths preventable from the point of view of operative timing or planning? Three deaths were due to prolonged hospitalization with operations on the twenty-second, twenty-ninth and thirtieth days of the disease. One patient was a fifty-three year old healthy man who entered the hospital with chills and fever, jaundice and a tender mass in the right upper abdominal quadrant. X-ray examination showed stones in the right upper quadrant. On the third hospital day a surgical consultant wrote: "I do not believe that operative intervention is indicated at this time but suggest waiting until the inflammatory process and cholangiolitis have quieted down." On the fifth hospital day or the ninth day of the disease, blood cultures were positive for B. coli. The patient became oliguric, uremic and more jaundiced. On the eighteenth hospital day, when the non-protein nitrogen was 219 mg. per cent and the icterus index 220, a cholecystostomy was performed with evacuation of white bile. Death occurred three days postoperatively with multiple liver abscesses.

Four patients died on the fifth day of their disease, but they had all been operated upon on the second hospital day. Two might have been saved if they had come to the hospital sooner, but the other patients had such advanced associated disease (cardiac decompensation and acute leukemia) that the time of operation would have had no influence.

The choice of operation may have had some bearing on the two deaths in which choledochostomy was performed with inadequate reason, thus prolonging the operating time on poor risk patients.

It is therefore possible that seven of these deaths might have been prevented by a better choice of procedure or earlier operation. This then would leave us with a possible over-all operative mortality rate of 6.5 per cent in a population such as this.

How does complicated gallbladder disease compare with uncomplicated acute gallbladder disease? Those patients with acutely diseased gallbladders had a mortality rate of 7.4 per cent, gangrenous gallbladders 20 per cent, and perforations 30 per cent. Of the perforations, nine were in localized pericholecystic abscesses, with two deaths (22 per cent); five were free and generalized, with four deaths (80 per cent); and six were free but localized to the right upper abdominal quadrant, with no deaths. It would

thus seem that the condition of the gallbladder was an important consideration in the mortality rate. Is it more so than the associated diseases? Ninety-four per cent of all the deaths occurred from associated disease and almost all the complications occurred in patients with associated vascular diseases. Six perforations and seven instances of gangrene occurred in patients with no associated disease and there were no deaths in this group of patients. It would thus appear that the associated disease and its care are factors which must not be lost sight of in planning treatment for patients with acute cholecystitis. Sufficient time must be taken in the workup of a patient to treat as adequately as possible the associated disease before surgery is performed.

SUMMARY

A series of 134 cases of acute gallbladder disease are reviewed pathologically and clinically. From the pathological point of view there is good evidence that gallbladders may be easily operated upon within the first ten days of an acute attack, and that the earlier this is done the less chance there is for subsequent perforations either by gangrene or infection.

An additional factor for early operation may be the prevention of an occasional case of B. coli septicemia which has an ominous significance.

The majority of the complications of gallbladder disease and deaths occur in the older age group or in those patients with associated disease. A more vigorous approach must be planned for this group.

The possibility of acute cholecystitis must be stressed in all patients with known biliary disease who enter a hospital for medical or surgical treatment. This may help to explain an occasional difficult diagnostic syndrome once therapy for the unrelated condition is begun. Cortisone must be added to the drugs to be feared in this regard.

Watchful waiting is difficult since there is a poor correlation between the signs and symptoms and the complications of gallbladder disease.

Laboratory aids are of some value, especially if correlated with the patient's age and associated vascular disease.

Of particular significance is an elevated right diaphragm, since when it is present it is associated with complicated gallbladder disease in a high percentage of cases.

The differential diagnosis should carefully rule out hepatitis, heart disease, pneumonia, pancreatitis and pyelonephritis.

The preferred operation is cholecystectomy with cholecystostomy reserved for the patient in poor general condition or for difficult pathological findings. Unless there are definite positive indications, exploration of the common duct is not advised, particularly in patients with associated vascular diseases.

The over-all mortality rate was 12 per cent and varied with the condition of the gallbladder and physical status of the patient. Early operation may control the condition of the gallbladder. Sufficient time must be taken before surgery to improve the physical status of the patient.

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DISCUSSION

E. EVERETT O'NEIL (Boston, Mass.): Thank you, Dr. Byrne, for an excellent paper. I am sure that some of the doctors from other parts of the country would like to comment on this and either agree or disagree with you.

ALEXANDER BRUNSCHWIG (New York, N. Y.): I think that Dr. Byrne has made a very important point. First, I agree with his general thesis that this is a situation which *a priori*, calls for immediate operation rather than temporizing. Now there are exceptions, of course, but in general I think that the immediate operation is to be desired.

As to rules and regulations, that is something else. I think that every surgeon who sees acute gallbladder disease—and I have seen much less of it than I used to—has his own ideas and I do not quite see how one can standardize the treatment.

We have to take into consideration surgical talent. I think that where good surgeons are present, one can consider immediate operation much more easily than if the best of surgical ability is not around. I would like to emphasize especially what Dr. Miller and others have said, that is, that cholecystectomy is a dangerous operation; and although the simplest one might look easy, it is fraught with danger and should be considered in that light.

DR. O'NEIL: You seem to be satisfied that cholecystectomy is a dangerous operation. What about performing cholecystectomy, let us say, on the seventh or eighth day of the disease?

DR. BRUNSCHWIG: I would, personally; but if there is more waiting to be done, I would wait much longer, until forced to operate.

If one is going to wait, the thing to do is to wait until the clinical evidence of the inflammation has subsided. No one has really shown that it is bad to let the lesions cool off.

DR. O'NEIL: I think that Dr. Byrne possibly might disagree with that point of view.

DR. BRUNSCHWIG: I know that there are still differences of opinion in this country. I do not know what the situation is going to be in the future, but we can still disagree.

DR. O'NEILL: Dr. Strauss, I am sure you have a word of discussion.

DR. STRAUSS: I believe that we have to individualize these cases. I agree with Dr. Byrne and I think many a patient has lost his life because we waited too long. I am inclined to believe that the average case, when you operate early, needs a cholecystectomy rather than gallbladder drainage. Occasionally there is some disease in the common duct; and if the patient is in good condition, I do not hesitate to open and drain that, too, because I think the patient recovers more quickly after the common duct is drained.

I agree with Dr. Byrne, but I think a good deal depends sometimes on the physical findings. Just recently I saw a case which was being treated conservatively. I happened to come along and see that the man had more pain. I performed a cholecystectomy and the patient recovered; but I do not think that the patient would have done very well if he had been left there and not operated upon.

I think that you do have to individualize the cases, depending on the temperature, rigidity and the reaction of the patient.

DR. O'NEIL: Dr. Dunphy, do you have any comments?

J. ENGLEBERT DUNPHY (Boston, Mass.): I would like to congratulate Dr. Byrne on a very careful and critical analysis of his material. I find myself in complete agreement with his conclusions.

The mortality rate obviously is too high, but it reflects the large number of patients over seventy-five years of age. As I glanced at the data I think there were several patients over eighty years of age. If patients under the age of sixty-five would go to their surgeon within the first twenty-four or forty-eight hours of the onset of symptoms, essentially there would be no mortality from this disease.

It is doubtful whether we in this hospital can attain the record of 1 or 2 per cent mortality comparable to that reported from other hospitals. It will require a great deal more cooperation on the part of the referring physician and the patient.

Our patient age groups are such that they do not come to the hospital until they are extremely ill. Having had the disease for several days, they pose an extremely difficult problem. The problem is, however, very challenging and rewarding from the point of view of surgical training and education.

The thing I would stress is what Drs. Miller and Byrne have said. Here is a real place for the skilled use of the planned cholecystostomy. We deal with the biliary disease at a later date.

DR. O'NEIL: Dr. Faxon probably sees a different group of cases.

HENRY FAXON (Boston, Mass.): I would like to add some comments. First, I want to say that I certainly appreciate the orderly presentation that has been made.

I should like to ask three questions. First, Dr. Byrne probably mentioned it but I failed to take it in, that although acute gallbladder disease is

caused by obstruction, what percentage of the gallbladders had stones?

DR. BYRNE: It was 92 per cent.

DR. FAXON: That is a good, crisp answer. However, I have been especially interested in the group of cases that followed surgery in related cases. We have had six cases in the last five years with unrelated disease, in which the patients were on parenteral feeding. Then on the seventh day acute cholecystitis developed, and in each instance there was a gangrenous gallbladder. In one of the worst of these cases, there were no stones and I wondered whether the etiology would be something other than the usual obstruction.

DR. BYRNE: Our patients all had stones, but I am sure the stasis of the gallbladder increased the viscosity of bile, which must play a role.

DR. FAXON: These patients had gone back to their oral feeding and suddenly the acute gallbladder disease developed.

DR. BYRNE: The disease is very common. Therefore there will be a certain number of people who have it when they are sick with something else.

DR. FAXON: Dr. Miller, do I understand that you should never attempt to remove a gallbladder from above downward without carefully identifying the duct and the artery?

DR. MILLER: That is correct. In acute gallbladder disease when there is considerable edema we like to remove the gallbladder from above downward, thus identifying the artery and duct a little more easily.

DR. FAXON: In those instances, you do remove the gallbladder really before you have oriented yourself with the common duct?

DR. MILLER: That is right. Usually you can tell whether you can dissect it.

LESTER B. WHITAKER (Portsmouth, N. H.): I am writing a paper, "Living Thirty Years among Gallstones," not *with* them.

I was amazed that no one made any comments on Dr. Miller's paper, especially since he advocated removing the gallbladder from below in all cases except those acutely inflamed and difficult, in which case you would take it from above. Now, if it is easier and safer to remove a badly diseased gallbladder from above, why is it not easier and safer to remove a simple gallbladder from above? I believe it is, and I hope that you will consider that and try it.

DR. O'NEIL: I think that you have many companions.

DR. WHITAKER: The difficulty, of course, is bleeding. The surgeon must know how to handle all degrees of bleeding. There is usually less bleeding when the gallbladder is removed from above. Also, electrosurgery is effective.

DR. O'NEIL: Are there any further questions?

QUESTION: I think that it is worth while to pause now and take into consideration the value of anesthesia. If I have any word to offer the young surgeon starting to treat acute cholecystitis, it is to make sure that good anesthesiologists are available at all times.

STEPHEN MEAGHER (Boston, Mass.): I would like to say that the lowest morbidity figures are associated with elective biliary surgery, especially in gallbladder cases, and probably this is the foundation of the hypothesis of conservative management of cholecystitis. The figures were not mentioned in this group. However, if one considers the postoperative pneumonias, hernias, eviscerations, and so on, you will find the incidence is greater in this hospital in patients of comparative age groups.

It is my own belief that almost all cases of acute cholecystitis can be controlled provided a regimen is advised and strictly adhered to. If you infringe upon that, you get an immediate return of symptoms.

There is common ground as far as diabetic patients are concerned and also persons with advanced arteriosclerotic disease. This type of case presents no argument. The patients ought to undergo cholecystotomy, at least.

N. FREDERICK HICKEN (Salt Lake City, Utah): At one time we had as Chief of Medicine at our hospital a man whom I greatly admired for his field of interest. He believed that surgery accomplished nothing in the management of any disease.

I took the opportunity of reviewing the cases of acute cholecystitis admitted to his service by mistake or through the oversight of the surgical house officers in the Emergency Room. His mortality was 38 per cent over a period of time. At the same time, the Surgical Service mortality rate was roughly comparable to Dr. Byrne's.

That is a good argument.

Secondly, in reviewing our experiences with cholecystectomy at our hospital, we performed 152 elective procedures in patients over sixty years of age without a single death, wound infection or any morbidity. Either we are lucky or I probably stopped the series at the advantageous time; nevertheless, it shows what an innocuous procedure cholecystectomy is. In spite of this a third of the patients give a history of ten years or more of prior gallbladder disease. Therefore the prevention of acute cholecystitis is something not mentioned here, and it should be an important part of management.

QUESTION: I wonder if anything is known about the possibility of pushing sand or stones into the common duct when the gallbladder is removed from above downward.

DR. O'NEIL: I am in possession of no facts on that score. Drs. Whitaker or Miller may have something for you. There is the possibility of

squeezing stones or gravel down into the common duct when you remove the gallbladder from above downward.

Dr. Whitaker: You probably will not squeeze the gallbladder any harder than you would in the normal emptying. As to the cystic duct, you dissect it carefully. The normal lumen is from 1 to 2 mm. in diameter. The cystic duct is very kinked, so that unless you have an abnormally dilated cystic duct there is no danger in squeezing down the stones in my opinion.

Question: I would like to ask Dr. Byrne to comment on one thing. The older patients with cholecystitis are reluctant to undergo surgery. We sometimes hope that we can close our eyes and these patients will get well and never return. Now, according to Dr. Byrne, these are the patients who need the early operations more than the younger patients.

Dr. Byrne: I really did not think there would be any discussion. I thought, after reading articles by Dr. Dunphy and others on the subject written ten years ago, that nothing much had changed. I believe these people should be operated upon as early as possible. If they are too ill or the disease is too severe, cholecystostomy is preferred; if not, a cholecystectomy. You cannot eliminate older patients, those with leukemia or diabetes, from the series. I am sure if you took them out of the groups you could do many things with acute gallbladder disease, but you cannot take them out. You have got to make an early approach.

The Problem of Retained Common Duct Stones

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Unfortunately the actual accomplishments of surgery often fall short of our hopeful desires. In spite of improved diagnostic facilities and excellence of surgical skills we must often accept defeat, or at least admit temporary failures. Such have been our experiences in operations upon the hepatobiliary system. We have been chagrined by our failure to open the bile ducts when they contained stones, and embarrassed by our inability to remove all of the calculi from the ducts which were explored.

The undesirable complication of "residual," "overlooked" or "missed" intraductal stones occurs with annoying frequency. Pribram [*23*] reported that 16 to 25 per cent of patients operated upon for choledocholithiasis still harbor intraductal calculi. Smith et al. [*27*] performed 224 cholecystectomies and choledochotomies and found that in twenty-four patients (10 per cent) all stones had not been removed. Thomson [*28*] re-explored the bile duct of 106 patients and was surprised to find that 11.6 per cent still had residual stones. Likewise, Singleton and Coleman [*26*] performed forty-three choledocholithotomies but failed to remove all calculi in three cases, an incidence of 9 per cent. Buxton and Burk [*8*] performed 190 choledocholithotomies, leaving residual stones in 8.3 per cent. They also explored the bile duct of 249 patients without finding stones, yet postoperative cholangiograms demonstrated retained stones in 3.6 per cent of their cases. Glenn [*10*] followed up 100 patients having cholecystectomies for gallstones, in whom the bile ducts were not explored, and found that within a ten-year period 4 per cent required secondary operations for residual choledochal stones. In performing 715 consecutive cholecystectomies for cholelithiasis, we explored the bile duct of 232 patients (32.4 per cent); choledochal stones were recovered from 105 patients (48 per cent). In four instances (3.5 per cent) we failed to remove all intraductal stones.

Why are not all calculi removed from the larger bile ducts during choledochotomy? In order to answer these questions the records of eleven local hospitals were studied, from which 150 instances of "retained" choledochal stones were found. The primary operations were performed by thirty-eight different surgeons, consisting of residents, occasional operators and certified surgeons. Residual stones were missed ten times more frequently by the occasional operator than by the well trained surgeon [*12*].

There are certain pathological conditions associated with cholelithiasis which seem to prevent the complete removal of all offending calculi:

Hepatolithiasis. Intrahepatic calculi are usually inaccessible and cannot be removed, yet they occur in 7.4 per cent of all cases of cholelithiasis, according to Beer [*3*], Best [*4*], and Hicken, McAllister and Call [*14*]. Hepatolithiasis was found in forty-two of our patients by operative cholangiograms, and in none of them were we able to remove all the stones. (Fig. 1.) In twenty-four instances the calculi were found in both lobes of the liver, in twelve cases they were confined to the left lobe only, and in six to the right lobe. One patient required four choledocholithotomies because the hepatic stones persisted in migrating down into the common duct and producing an obstructive jaundice. The last operation was performed eight years ago and she is enjoying good health in spite of the fact that she still has many intrahepatic stones. Because the surgeon can seldom

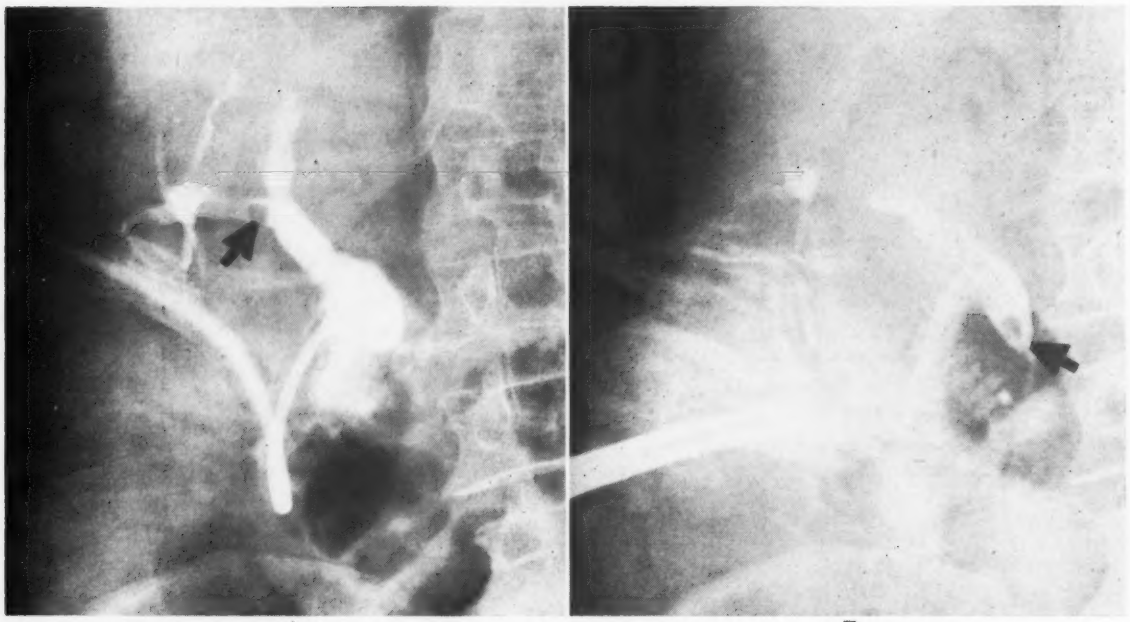

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FIG. 1. A, four stones were removed from the common duct and the sphincter was dilated. The postoperative cholangiogram shows an "overlooked stone" in the right hepatic duct and obstruction of the ampulla due to pancreatic edema and swelling. B, seven days later the right hepatic stone had migrated to the ampullary portion of the common duct. Because of the narrowing of the terminal portion of the choledochus, this stone was recovered at a second operation.

localize, let alone remove, liver stones this particular phase of "retained" calculus seems insoluble.

Small Stones. Experience indicates that it is difficult to rid the bile ducts of biliary sand and small calculi. Unless the stones are of a sufficient mass they do not impart an impact, or produce a "sense of scraping," when coming in contact with the exploring scoops, forceps and probes; hence the surgeon is unable to detect their presence. On many occasions we have thought all the stones had been removed from the bile ducts and, on "passing the scoop once more just for good luck," another elusive stone rolled out. Likewise, we have persistently and thoroughly irrigated the bile duct to be certain that all bile-sand had been flushed into the duodenum and, while talking to the resident, have seen an unexpected stone float out of the ductal incision. Small calculi can be missed, as evidenced in Figure 2.

Encysted Stones. Sometimes stones become loculated in diverticular sacs of the bile ducts and, as they do not encroach on the ductal lumen, instruments may be passed along the ducts without ever coming in contact with calculus. If these stones are small they cannot be detected by palpation. Because they do not obstruct the common duct there is no attendant jaundice; hence the clinical indications for ductal exploration are absent. Operative cholangiograms afford the best method, for discovering these misplaced calculi. Occasionally inspissated bile and "sand" obstruct the cystic duct but are not large enough to be detected by palpation, hence are often overlooked. Such stones can and do cause symptoms. (Fig. 3.)

Impacted Stones. Under certain circumstances gallstones may become impacted in the terminal portion of the choledochus where resulting ductal fibrosis and inflammation intensify their incarceration. If grasping forceps are applied to such a calculus the force necessary to extract the stone may be sufficient to break it into small pieces. The sharp fragments may be driven into the ductal wall, only to produce tissue irritation, and later escape into the ductal lumen. Sometimes these fragments float around in the bile and cannot be flushed out by ductal irrigations or removed by scoops. These small sand-like particles form an excellent nidus for the formation of new stones.

Speed. Another factor which contributes to "retained" choledochal stones is the tendency to rush through operations. It requires time to expose the bile ducts adequately, explore their

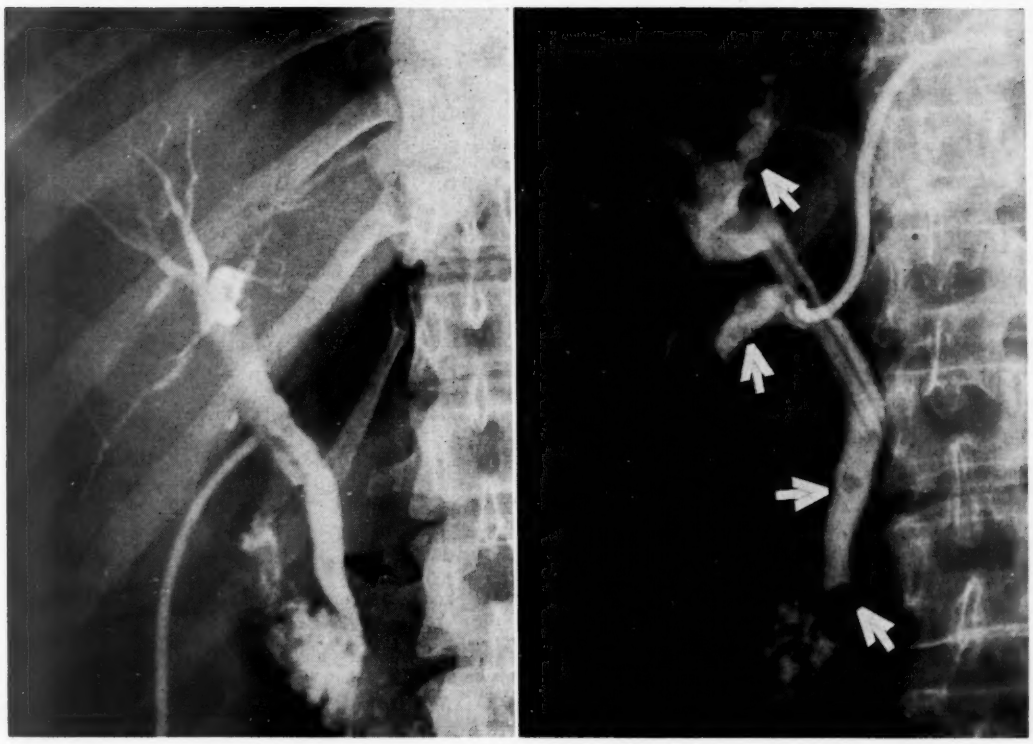

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FIG. 2. Five stones were removed from this common duct but one small calculus was "missed."

FIG. 3. Postoperative cholangiogram outlines "overlooked" stones in left hepatic, common hepatic and choledochal ducts. The dilated stump of the cystic duct contains stones.

lumen, extract contained calculi, lavage the intrahepatic radicles and dilate the ampulla of Vater. Additional time may be needed to perform plastic procedures upon the stenotic ampullary orifice. If the patient has been improperly prepared or if he is a poor operative risk, the surgeon may be unable to take the necessary time to perform these corrective procedures. Figure 4 is a choledochogram of a patient who has had three operations for "reformed" or "residual" choledochal stones all because the strictured ampullary segment of the common duct was not dilated at the primary operation. Such stenotic lesions can be best corrected by transduodenal ampullotomy or hepaticojejunostomy.

Patients with cholelithiasis are seldom so acutely ill that ample time cannot be taken to prepare them for the added trauma of surgery. Even when dealing with acute cholecystitis it is not necessary to perform "middle of the night" operations. Figure 3 represents the extrahepatic system of a patient with acute cholecystitis and jaundice. She was rushed to surgery. The gallbladder was removed and the common bile duct was found to contain stones. Just as the ducts were to be explored the anesthetist urged the surgeon to terminate the operation; hence a decompression tube was inserted into the common bile duct and the abdomen was closed even though stones were knowingly left behind. Nine years later she was compelled to submit to a second operation, and the operative cholangiogram denoted a dilated bile duct filled with many stones. Proper preparation of the patient should have permitted all offending stones to be removed at the primary operation.

DIAGNOSIS

No one will contradict the statement that every bile duct which contains stones should be opened and thoroughly explored. The enigma is, which ducts harbor calculi? Unfortunately the conventional criteria for choledochotomy are not infallible.

For example, the size of the common duct is not an accurate guide for exploration as many dilated ducts do not contain stones, while normal or small-sized ducts may. Palpation is not infallible as Buxton and Burk [*8*] were able to palpate only 48 per cent of the choledochal

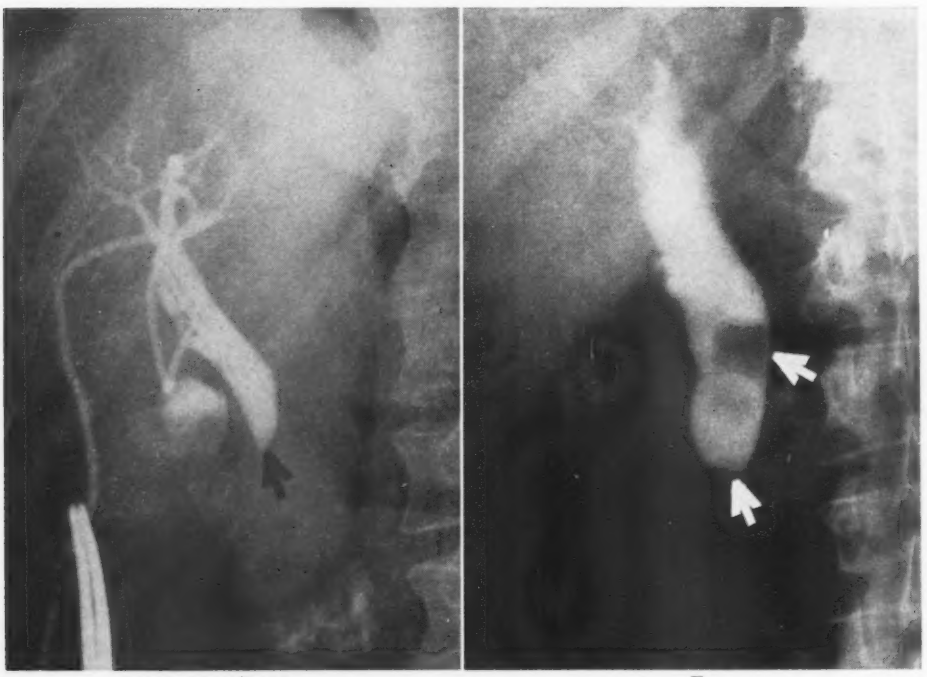

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FIG. 4. A, seven stones and some biliary sand were removed from the common duct. The postoperative cholangiogram demonstrates a stenosis of the terminal portion of the choledochus. B, eight months later the patient returned with obstructive jaundice. The operative cholangiogram outlines two large stones and obstruction of the ampulla. Choledocholithotomy and transduodenal ampullotomy were employed.

stones they removed. This means that 52 per cent of the calculi were either too small or located in such a position that they could not be detected by the palpating fingers. Jaundice is not an accurate indication for choledochotomy as only 60 per cent of our 150 cases exhibited hyperbilirubinemia even though the ducts contained stones. Examination of the statistics from the larger surgical centers, where well trained surgeons work, indicates that only 20 to 50 per cent of the choledochotomies yield calculi. In simpler terms, the conventional indications for ductal exploration were misleading in 50 to 70 per cent of the cases. Unfortunately the indications for choledochotomy vary with the enthusiasm and experience of the surgeon, and not until some exact method of diagnosis and localization of intraductal stones are available will these errors be minimized. As yet we have no such procedure.

Operative Cholangiography. Since 1936 we have employed operative and postoperative cholangiography as a routine procedure in more than 1,800 hepatobiliary operations. By injecting suitable contrast media into the gallbladder and bile ducts during the operation, the surgeon obtains an accurate radiographic pattern of the entire biliary system. He has a "blueprint" of the problems to be solved. Pathologic lesions such as stones, kinks, strictures and neoplasms produce recognizable deformities. Anatomic variations in size, shape and position of the bile duct can be quickly recognized. This form of examination is not intended to supplant the conventional methods for determining the functional status of the bile ducts, such as inspection, palpation and instrumental exploration, but is rather a valuable complementary procedure.

Cholangiograms provide additional information by showing which ducts are normal (hence do not need to be explored) and designating those which should be opened. In 106 choledocholithotomies we were able to palpate but 52 per cent of the stones which were removed, indicating that 48 per cent of the calculi were located by cholangiograms. It is interesting that in forty-two instances the cholangiograms outlined intrahepatic stones which could not be detected by any other method. This agrees with the experiences of Mehn [20] who found ten unsuspected stones in 113 cholangiograms.

Baker [2], Mixter, Hermanson and Segel [21], and Hoerr [15] emphasize that operative cholangiograms are not only useful in determining the presence of intraductal stones but also very helpful in ascertaining which ducts are normal, thus eliminating unnecessary ductal explorations. Like all diagnostic procedures, however, cholangiography has its limitations, is occasionally misleading and at times absolutely uninformative, but what radiologic procedure is not, whether it be a urogram, an encephalogram or an x-ray study of the gastrointestinal tract. Experience and precision do much to reduce the percentage of errors.

Completion Cholangiograms. Whenever the common bile duct has been opened and explored the surgeon is always anxious to know if all offending calculi have been removed. Such information can be obtained by injecting the T tube with a suitable contrast medium and obtaining a choledochogram while the abdomen is still open. Thomson [28] used completion cholangiograms in all choledocholithotomies and was compelled to remove the T tubes and re-explore the ducts because of retained calculi in 25 per cent of his cases. We have discovered "overlooked" stones by this method in ten instances, and have removed the T tubes and extracted the elusive calculi. It is much better to detect the residual stone at the primary operation than be compelled to subject the patient to a second exploration.

Postoperative Cholangiography. The only method for determining whether all stones have been removed from the bile ducts is to employ postoperative cholangiograms. The clinical course provides no index as to the completeness of the primary choledocholithotomy. In more than 80 per cent of our 150 cases the patients were well enough to leave the hospital, even though it was known that their bile ducts contained stones. Partington and Sachs [22] maintain that every patient with a drainage tube in the common duct should have a cholangiogram before the tube is removed. As a rule these cholangiograms can be obtained on the sixth or seventh postoperative day and the surgeon then knows whether the ducts are normal or if they are obstructed by stones.

Intravenous Cholangiography. Intravenous cholangiography is particularly useful in detecting the presence of retained stones which produce symptoms after the wounds have healed. McClenahan, Evans and Braunstein [19] studied 121 patients with "postcholecystectomy" complaints and were able to visualize the bile ducts in 105 instances, finding intraductal calculi in eleven cases (9 per cent). Interestingly they discovered calculi in ducts having a normal diameter or caliber. Glenn [11] recommends intravenous cholangiographic studies of all patients having choledocholithotomies at intervals of one, two and three years. He believes it takes time for the small overlooked calculi to enlarge sufficiently to be recognized by this method. Unfortunately such studies cannot be employed in the presence of jaundice, cholangitis, hepatitis, cirrhosis of the liver or in critically ill patients; hence their diagnostic usefulness is somewhat limited.

The loss of bile through an external biliary fistula usually signifies ductal obstruction. If the sinus tract is injected with radiopaque material the dilated ducts and offending stones can often be visualized. Residual stones may be found in the sinus tract, the choledochus, the common hepatic bile duct and the intrahepatic radicles.

The diagnosis of "retained," "residual," "overlooked" and "missed" intraductal stones can be accurately made, providing diagnostic facilities now available are employed.

TREATMENT

When the postoperative cholangiograms demonstrate the bile ducts to contain residual calculi, what happens to the unfortunate patients? A partial answer to such a question was obtained by following the clinical course of 150 patients so affected. Information obtained from questionnaires sent to the patients, from letters of inquiry answered by participating surgeons and from facts obtained by direct examination of many of the patients provides the data for this report. The time interval covered by this study ranged from one year to eighteen years. The diagnosis of "retained" calculus was made by the radiologist from postoperative cholangiograms which were obtained by injecting contrast media into indwelling T tubes during the period of primary hospitalization. The diagnosis was positively confirmed in 126 cases (84 per cent) either by operative or autopsy findings. Twenty-four patients, however, were known to have retained stones and either refused additional treatment

or died from unrelated diseases on which no autopsy reports could be obtained.

For practical purposes all of these patients were subdivided into three therapeutic groups: (1) those having the problem of "retained" intraductal stones solved during the period of primary hospitalization; (2) those who were released from the hospital but returned at a later date for ductal surgery; and (3) those who refused further surgical treatment.

The *primary group* consisted of thirty patients (20 per cent) who had their problem of "retained" stones solved during the period of primary hospitalization. In twenty instances persistent jaundice, severe biliary colic, draining biliary fistulas, subhepatic abscesses, subphrenic abscesses and bile peritonitis necessitated re-exploration with removal of the offending stones. There were no operative deaths in this group.

There were ten patients, however, whose postoperative cholangiograms on two or more occasions clearly outlined intraductal stones, but subsequent x-rays failed to detect their presence. It was assumed that these stones had been dissolved or had passed spontaneously through the ampullary outlet into the intestinal tract. This is not an unusual occurrence for Johnston et al. [17] described twelve cases of retained intraductal stones; in six patients the calculi passed spontaneously into the intestinal tract, and the remaining six required reoperation. Singleton and Coleman [26] have reported similar experiences. Retained calculi are much more prone to pass through the ampulla if transduodenal ampullotomy has been performed.

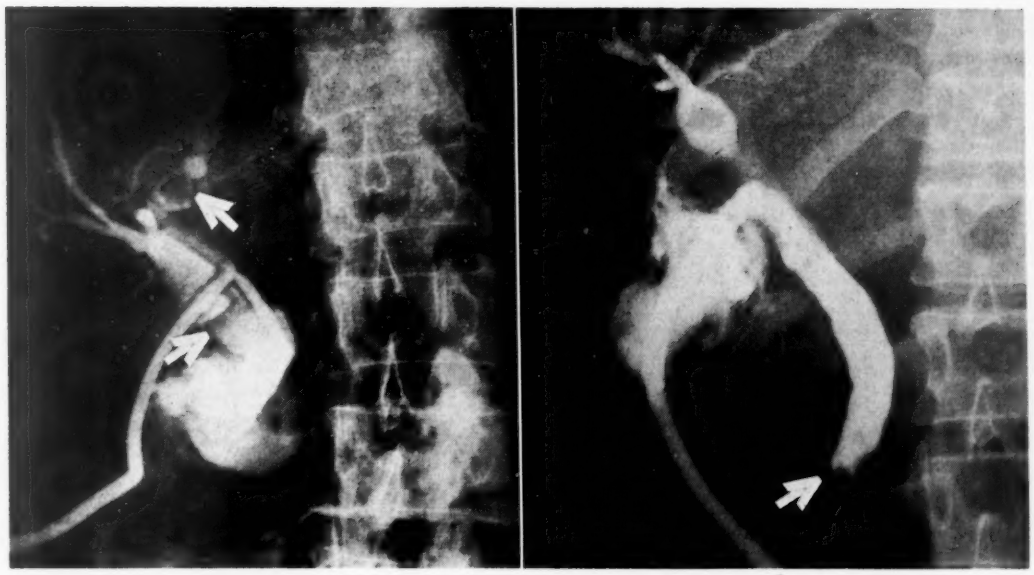
In the *delayed group* 120 patients were released from the hospital following choledochotomy, even though it was known that the larger bile ducts harbored residual stones; ninety-six returned for removal of the obstructive calculi. The time interval between the first and second operations varied from one month to eighteen years. One patient suffered from a persistent draining biliary fistula for eleven years before seeking relief. Nausea, vomiting, jaundice, pain, weight loss, fistulas and malnutrition were the complaints from which the patient sought relief. In eighty-four instances all of the offending calculi were removed at the second operation, but ten patients required three explorations and two required six choledocholithotomies each. These ninety-six patients had a total of 126 operations with a mortality rate of 3.8 per cent.

In the *resistant group* twenty-four patients refused further surgical therapy for various reasons: eight were so comfortable they felt no need for a second operation, another group of eight patients were so frightened from the original surgery that they refused additional surgery in spite of annoying complaints, and eight died of unrelated diseases before the biliary complications assumed serious proportion.

It is obvious that given ample time intraductal calculi invariably produce undesirable symptoms and complications, as 85 per cent of our patients required secondary corrective operations. Glenn [10], Ravdin [25], and Buxton and Burk [8] believe that residual intraductal stones should be removed as soon as they are recognized, providing that the patient's condition permits it.

Non-operative Management. When confronted by retained ductal stones it is only natural that the surgeon would seek some method, other than reoperation, to remove the unwanted calculus. Three plans have been developed: (1) chemical dissolution or fragmentation of the stones; (2) mechanical flushing of the calculi from the bile ducts into the duodenum by positive pressure ductal irrigations; and (3) physiologic hydrochloretic flushing of the ducts. In actual practice a combination of these methods has been tried.

Chemolysis: Gallstones consist of cholesterol, calcium salts, bilirubin pigments and cellular detritus. The admixture of these components varies in different forms and stones. It is obvious that any substance or solvent which would dissolve, extract or absorb any of these constituents could result in the dissolution, disintegration or fragmentation of the stones. Many agents have been used, such as ether, ether-alcohol and chloroform mixtures, with the hope that they would extract the cholesterol from the stones. Agents which lower the surface tension, such as detergent-Sorlate,® bile acids, bile salts and animal bile, have been employed with the belief that they penetrate or "seep" into the stone and thus facilitate its disintegration. Calcium binding agents, such as versene and citrates, were used because of their effects in disturbing the relationship between the insoluble calcium salts and the calcium ions. If the agent could draw away the calcium ions and bind them in some other soft materials then



5 6

FIG. 5. Attempts to dissolve the intrahepatic and ampullary stones by instillations of ether and chloroform were ineffectual. Calculi were removed at a second operation.

FIG. 6. An attempt to dissolve the intrahepatic stone and the large calculus in the common duct was unsuccessful, even after ten treatments with chloroform.

the stone might be fragmented. Naturally occurring fatty acids, both the saturated and unsaturated types, have been employed because *in vitro* experiments indicated they assisted in disintegrating the stones. Hydrotrophic agents, such as bile salts, bile acids and animal bile, have been thought to render cholesterol and fatty acids more soluble. Enzymatic agents such as trypsin, Caroid® and hyaluronidase were found to be of use in removing the mucilaginous protecting covering of the stones and thus permitting the chemolyzing solution to effect disintegration. Dispersing agents, such as marasperes, function by absorbing out solid particles and dispersing them by polar action. Many other agents, such as strong acids, weak acids and boiling water, have been utilized but the majority of these substances have little therapeutic value.

Walker [*29*] in 1891 introduced ethyl ether through a cholecystostomy sinus and successfully dissolved a stone impacted in the cystic duct. Sporadic reports as to the efficacy of this method appeared in the literature but it remained for Pribram [*23*] in 1934 and again in 1947 to revive interest by reporting the dissolution of "residual" gallstones in fifty-one cases. He attributes his success to the fact that the ether was placed in direct contact with the stone by a "slow drip" instillation, thus keeping the solvent in contact with the calculus for a sufficient period of time to effect dissolution. This requires persistence, patience and time. We employed the ether instillation in fifteen patients with residual stones and were successful in only one instance. Perhaps our failures were due to lack of perseverance but many patients would not submit to repetitive installations. (Fig. 5.)

Chloroform is an excellent solvent for cholesterol and if heated to 61°C. (141.8°F.) it rapidly penetrates the gallstones, thereby causing disintegration. Best, Rasmussen and Wilson [*6*] reported excellent results in fourteen patients. They stress the advantage of agitation obtained by injecting, aspirating and reinjecting the heated chloroform through a T tube. Singleton and Coleman [*26*] likewise favor the use of chloroform and believe that many overlooked ductal stones can be safely dissolved by this method. Best, Rasmussen and Wilson [*6*] insist that the solubility of the stones removed at the time of cholecystectomy should be tested *in vitro*, and the most effective solvent should be selected to dissolve the retained stones.

These chemolyzing treatments are not without danger, for Burgess [*7*] reported that excessive vaporization pressures of ether have resulted in injury to the liver. Probstein and Eckert [*24*] observed the sloughing of duct

epithelium in dogs receiving ether through a cholecystostomy tube. Amsterdam and Sterling [*1*], on the other hand, used daily instillation of ether for a period of eleven months without noting untoward effects. It is common experience, however, that the high volatility of both ether and chloroform produces such high intraductal pressure that patients are nauseated, often vomit, experience severe colicky pains and often pass into a state of shock. Both Pribram [*23*] and Best [*6*] attempted to eliminate these distressing symptoms by employing a double-lumened T tube. One channel of the tube was used for injecting the solvent while the other acted as a vent to permit escape of the volatile fumes. We have employed the heated chloroform instillation in sixteen patients with residual common duct stones and have had excellent results in four patients. Again, our lack of enthusiasm for this procedure undoubtedly accounts for our high percentage of failures. (Fig. 6.)

Mechanical flushing of the bile ducts: It is quite obvious that if the choledochus contained small stones or biliary gravel these undesirable substances might be flushed from the bile ducts by using cleansing irrigations through an indwelling T tube. Such a plan would be more effective if the sphincter of Oddi were relaxed so the ductal outlet would not be obstructed. This has been accomplished by using spasmolytic drugs, such as amyl nitrate, nitroglycerine and papaverine hydrochloride, or by applying such anesthetic agents as Pontocaine,® Metycaine® and Nupercaine® directly to the sphincter by ductal instillations. This method has been very effective in cleansing the ducts of blood clots, gravel and stones having a diameter of less than 2 mm.

Physiologic flushing of the bile ducts: As early as 1892, Naunyn demonstrated that if human gallstones were placed in the gallbladder of dogs they slowly disappeared in the course of several months. Lutton and Large [*18*], working with sheep, goats and pigs, substantiated this phenomenon. Animal bile, being low in cholesterol content, slowly absorbs the cholesterol from the human gallstones, causing them to fragment and disappear. Appreciating this fact, Best and Hicken [*5*] in 1938 suggested the use of hydrochloretic agents as a method of increasing the production of hepatic bile, which being more dilute than normal bile might rid the bile ducts of retained debris. In numerous reports the "physiologic biliary flush" has been advocated, the latest being by Best, Rasmussen and Wilson [*6*]. Studies indicate that hydrochloretic agents increase the volume output of dilute bile by 100 to 250 per cent above normal. Johnston and Nakayama [*16*] reasoned that if the liver produced this dilute bile and if it continued to flow over the retained stones, there would be a gradual absorption of the stone-cholesterol; hence fragmentation would result. Unfortunately the hydrochloretic stimulation of the liver produces a dilute bile which has a cholesterol content equal to that of normal bile; therefore there is little influence on the stones. Johnston and Nakayama [*16*] treated two patients with sufficient hydrochloretic compounds to maintain an increased flow of bile for nine to thirteen months without there being any appreciable effect on the retained calculus.

Cole [*9*], accepting this thesis, studied nine patients with residual stones who also had T tubes in their common ducts. He used hydrochloretic agents to increase the flow of bile and then followed the rate of stone absorption by progress cholangiograms. In one instance it required eleven months for the stones to disappear. This seems to be a slow process, particularly if the patient is a wage earner.

We routinely employ the "physiologic biliary flush" in all cases of cholelithiasis, even though the bile ducts have not been explored. The increased flow of dilute bile seems to rid the ducts of blood clots, gravel and cellular detritus but has little effect on retained stones.

COMMENTS

It must be remembered that it is not the desires of the surgeon or the wishes of the patient which determine the type of treatment to be employed for residual intraductal stones. It is the condition of the patient and the nature of associated pathologic processes. Any attempt to dissolve stones or mechanically flush them into the duodenum is contraindicated: (1) if the calculus completely obstructs the bile ducts; (2) if the stones are larger than 2 mm. in diameter; (3) if the stones lie above the proximal limb of the T tube or within the intrahepatic radicles; (4) if the stone is in a diverticular pocket; (5) if the patient has severe pain; (6) if there is a persistent jaundice; (7) if there is cholangitis, subhepatic abscess or bile peritonitis; (8) if the patient's general condition is

unsatisfactory; (9) if there is an excessive loss of bile, pancreatic ferments and enzymes through the T tube; and (10) if the patient is anxious to assume occupational activities. All of these contraindications are self-explanatory and of necessity limit the usefulness of the non-operative management of retained stones.

Re-exploration of the bile ducts to remove the retained calculi should be attempted as soon as the patient's condition permits. It is a mistake to prolong the period of convalescence by having the patient go home, only to return several months later for definitive surgery. Particular attention should be given to electrolyte balance, blood volume, blood proteins and any signs of liver dysfunction. Any abnormalities should be corrected, if possible. The patients tolerate the operations better if they have been ambulatory for a few days.

The indwelling T tube provides an excellent guide to the common bile duct, so little difficulty need be experienced in isolating this structure. By using operative cholangiograms the position and number of offending calculi can be accurately determined. Again, we wish to re-emphasize the value of the completion cholangiogram in determining whether all stones have been removed. In our series the failure to remove all calculi at the second operation was because the stones occupied the inaccessible intrahepatic ducts. At present this problem is insoluble.

Surgical exploration is mandatory in those patients suffering from intractable jaundice, severe pain, subhepatic abscesses or bile peritonitis. Procrastination usually results in death. The risk must be accepted.

The best treatment for residual intraductal stones is to remove them at the primary operation. While highly feasible, accomplishment is next to impossible. We can, however, greatly minimize the incidence of this complication by adhering to the following: (1) Insist that those surgeons operating upon the extrahepatic biliary tract have special training in anatomy and ductal surgery, thus enabling them to recognize anatomical variations and to cope with unexpected problems. (2) Employ operative cholangiograms to detect ductal abnormalities, localize the stones, denote the strictures and test the patency of the bile ducts. (3) Use completion cholangiograms before closing the abdomen to make sure all offending stones have been removed.

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DISCUSSION

John J. Byrne (Boston, Mass.): Is there any discussion on this paper?

Question: I should like to ask Dr. Hicken if he considers cholesterol a binding agent, and is the dissolution of this substance the most important factor in the chemolysis of gallstones?

Dr. Hicken: As a rule, gallstones are composed of varying amounts of cholesterol, calcium salts, bile pigments, cellular detritus and mucilaginous materials. Cholesterol, being very soluble in ether and chloroform, can be more readily extracted than the more stable calcium salts. If the cholesterol can be removed, the stone disintegrates and the residue can be flushed into the duodenum.

Question: Has anyone tried using short-chain hydrocarbons to dissolve gallstones? They are nontoxic and are very effective in dissolving cholesterol the stones.

Dr. Hicken: I have had no experience with hydrocarbons as solvents for residual stones. Your idea is very good and merits investigation. Most short-chain hydrocarbons are not very volatile; therefore, they should not produce high intraductal pressure which is so characteristic of ether or chloroform.

Lester B. Whitaker (Portsmouth, N. H.): I should like to ask Dr. Hicken why he does not perform transduodenal sphincterotomies when there is narrowing of the choledochal outlet?

Dr. Hicken: We have employed sphincterotomies in selected cases, but do not advocate their use in cases of mild ductal stenosis because of the dangers arising from duodenal fistula.

Dr. Whitaker: I should like to argue for sphincterotomy just the same.

Dr. Byrne: Occasionally we have encountered duodenal fistula as a complication of sphincterotomy. There must be a definite indication before this operation is employed.

Question: Do you employ operative cholangiography as a routine procedure, even when performing a simple cholecystectomy?

Dr. Hicken: How can you tell which case of cholelithiasis will be simple and which will be complicated? As Dr. Miller has emphasized in his excellent paper on anomalies of the extrahepatic biliary system, at least 25 per cent of the population exhibit variations in both vascular and bile duct patterns. Such aberrations can be readily recognized by cholangiograms. Likewise, we were able to detect the presence of some stones which could not and would not be located by palpation. Cholangiography does not supplant the other methods of ductal exploration but is a complementary procedure.

Question: How often do you get "air bubbles" in the bile ducts when you are performing cholangiography?

Dr. Hicken: Remember that any air found within the bile ducts has been introduced during the process of injecting the contrast medium. It is imperative, therefore, that the cystic duct catheter or the common duct tube be irrigated with saline, so as to displace the air before introducing the radiopaque materials. Should there be any question as to differentiation between an intraductal air bubble and the stones, merely repeat the cholangiograms and compare the two films. Stones will be present on both cholangiograms, while air bubbles will have shifted their positions or passed through the ampulla into the duodenum.

Dr. Byrne: The Cleveland Clinic was mentioned as having used cholangiography. You should rise, Dr. Britton, in defense.

Richard C. Britton (Cleveland, Ohio): We employ both operative and postoperative cholangiography in all cases of biliary tract surgery at the Cleveland Clinic. We follow the method introduced by Dr. John A. Gius of Iowa, which consists of intubating the cystic duct with polyethylene tubing and using this to introduce the contrast media into the common bile duct. Such a plan minimizes the extravasation of the radiopaque materials into the periductal tissues, and thus provides clear ductal patterns. If you believe you will need the gallbladder for a by-passing operation, the cholangiogram can be obtained without any damage to the gallbladder itself.

One thing that characterizes surgeons is that they do not trust any one but themselves. As we viewed the films presented by Dr. Hicken, we all said to ourselves, "Well, if I had performed that operation, I would have removed all the stones"; yet in our own experience we have all missed intraductal stones.

I should like to ask several questions. Since you are never quite sure whether the common duct is completely "clean," when you go back the second time to remove stones, do you believe that sphincterotomy alone creates an adequate channel for

the passage of small stones (3 mm. or less)? Will contraction of the duodenal musculature obviate the benefit of sphincterotomy? Would you consider performing side-to-side choledochoduodenostomy in such a situation?

DR. HICKEN: Personally, I am not a proponent of sphincterotomy, because the incised sphincter of Oddi soon heals and the resulting scar tissue merely re-establishes the ductal obstruction. The sphincter of Oddi is very narrow, and if the ductal incision is more than 2 mm. in length it may injure the wall of the duodenum, resulting in annoying fistulas. If the terminal portion of the bile duct is stenosed or narrowed, I prefer to employ side-to-side choledochoduodenostomy or Roux-Y choledochojejunostomy rather than depend on sphincterotomy.

QUESTION: When would you employ side-to-side choledochoduodenostomy?

DR. HICKEN: I would perform this procedure if I had a poor-risk patient in whom time was an important element and in whom I could adequately decompress the biliary tree by anastomosing the choledochus to the duodenum.

QUESTION: I want to ask if choledochotomy increases the postoperative mortality.

DR. HICKEN: It most certainly does. Whenever the common bile duct is opened and explored there is always danger of injuring the ducts or producing hemorrhages, and even inviting bile peritonitis.

QUESTION: How frequently do you leave residual stones in the bile ducts, even though you use cholangiograms?

DR. HICKEN: In our series of 150 cases in which the bile ducts were explored, we overlooked stones in 3.2 per cent of the cases. We used operative cholangiograms to locate the elusive stones. We employed completion cholangiograms before closing the abdomen, and reopened some ducts and removed the stones; yet in spite of all these precautions we left stones in the liver and the bile ducts. At the present time we have no method which will assure complete removal of stones from the extrahepatic biliary system. We can greatly improve our present results by training and study.

DR. BYRNE: The amount of discussion we have had is evidence of the fact that everyone has left stones in the common duct.

End of Symposium on Biliary Surgery

Multiple Simultaneous Complications of Peptic Ulcer

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The three major, and at times catastrophic, complications of peptic ulcer are perforation, hemorrhage and obstruction. We have become interested in those patients who suffer two and even all three of these disasters simultaneously.

In reviewing the enormous surgical literature concerning these three complications, one is struck by the paucity of reports on their combinations in the same patient. Many authors even say that the perforated ulcer never bleeds and the bleeding ulcer never perforates. Probably because of its dramatic nature and high mortality the most frequently discussed of these multiple catastrophes is perforation with hemorrhage. Winters and Egan [*16*] found this combination in 10 per cent of their series of peptic ulcer perforations and in 1.5 to 18 per cent of other reported series. Estes and Bennett [*4*] reported hematemesis or melena near the time of perforation in 26.8 per cent of their patients, but in only two cases (2 per cent) at the time of perforation. Turner [*15*] reported the high figure of eleven massive fatal hemorrhages among 209 perforations. In his large experience, Finsterer [*5*] was confronted with combined perforation and massive hemorrhage in only four patients, three of whom died. Reviewing several series of perforations, Ivy [*12*] found a 6 per cent incidence of concurrent hemorrhage and said that sufficient data were lacking to establish the mortality rate from this combination. In 567 patients with hemorrhage, Baker [*1*] found only five with perforation, all of whom died. In addition, seventeen had associated obstruction, with eleven fatalities, and only one had the triple combination of perforation, hemorrhage and obstruction, with a fatal result. Beyond these, concise statements concerning the incidence and distinctive features of these serious combinations are hard to find and further study was therefore undertaken.

CRITERIA

It is obvious that the terms perforation, hemorrhage, and obstruction of peptic ulcers are capable of very broad interpretation, leading to confusion when one seeks to compare the various series. In the present study, the following criteria were used:

Perforation. This criterion was the finding of an acutely perforated peptic ulcer, either at laparotomy or autopsy; subacute or chronic perforations were not included. The presence of tumor or any other lesion of the esophagus, stomach or duodenum besides proved peptic ulcer was cause for exclusion.

Hemorrhage. This included: (1) the presence of hematemesis or melena verified by observation in the hospital; or (2) an anemia of sufficient severity to require at least one transfusion of 250 or 500 cc. and thought to be caused by recent hemorrhage of peptic ulcer; or (3) autopsy findings of at least 100 cc. of blood from acute or chronic peptic ulcer. Positive chemical tests for blood in the stool without melena were not included.

Obstruction. This category included (1) at least one gastric residual of 200 cc. or more of

non-bloody material prior to any surgery; or (2) gastric residuals of 200 cc. or more for at least five consecutive days following plication for perforation; or (3) the findings of pyloric obstruction on gastrointestinal series. Stomal obstructions in the convalescent period following gastric resection were not included.

STATISTICS

Between January 1, 1940, and March 1, 1957, there were 969 admissions to the surgical wards of The New York Hospital for perforated, bleeding or obstructed peptic ulcer. (Table 1.) This group consisted of 775 different patients. Of these admissions, eighty-nine (9.2 per cent) representing eighty-two different patients presented a combination of two or three complications. The remaining 880 admissions presented only a single perforation, hemorrhage or obstruction.

Of the eighty-nine admissions for multiple entities, there were: (1) twelve for combined perforation and hemorrhage (1.2 per cent of total admissions, 13 per cent of admissions for multiple entities); (2) fifteen for combined perforation and obstruction (1.5 per cent of the total, 17 per cent of the admissions for multiple entities); (3) fifty-seven for combined hemorrhage and obstruction (5.9 per cent of the total, 64 per cent of the admissions for multiple entities); and (4) five for combined perforation, hemorrhage and obstruction (0.5 per cent of the total, 5.6 per cent of the admissions for multiple entities).

In the entire study there were 152 patients with perforation, 678 with hemorrhage and 233 with obstruction. In the multiple entity group, there were thirty-two with perforation, seventy-four with hemorrhage and seventy-seven with obstruction. Thus, 21 per cent of all patients with perforation suffered concurrently one or two other complications, as did 11 per cent of all with hemorrhage, and 33 per cent of all with obstruction.

TABLE 1
MORTALITY STATISTICS—SINGLE AND COMBINED COMPLICATIONS OF PEPTIC ULCER

Group	No. of Cases*	No. of Deaths	Per cent
Single entities	880	36 } 51	4 } 5.3
Multiple entities	89	15 }	17 }
Perforation and hemorrhage	12	6	50
Perforation and obstruction	15	4	27
Hemorrhage and obstruction	57	4	7
Perforation, hemorrhage and obstruction	5	1	20

* Nine hundred sixty-nine admissions of 775 different patients, including eighty-nine admissions of eighty-two different patients presenting a combination of two or three complications.

TABLE 11
AGE DISTRIBUTION—ADMISSIONS FOR MULTIPLE SIMULTANEOUS COMPLICATIONS OF PEPTIC ULCER

Age	No. of Cases*				
	Perforation and Hemorrhage	Perforation and Obstruction	Hemorrhage and Obstruction	Perforation, Hemorrhage and Obstruction	Total
10–19	..	..	..	..	..
20–29	1	..	..	..	1
30–39	1	7	2	..	10
40–49	1	..	11	2	14
50–59	5	6	13	1	25
60–69	2	1	15	1	19
70–79	2	1	11	1	15
80–89	..	..	4	..	4
90+	..	..	1	..	1
					89*

* Eighty-nine admissions (eighty-two patients) including eighty-one admissions of men (91 per cent) and eight admissions of women (9 per cent).

Sex and Age. There were eighty-one admissions of men (91 per cent) and eight admissions of women (9 per cent) in the multiple entity group. Table 11 shows the distribution according to age of patient. The decade between ages fifty and sixty was the commonest for these disorders.

Duration of Symptoms. Chronicity of ulcer complaints was a prominent feature of the multiple entity group, 25 per cent of the admissions having had symptoms for more than ten years. However, 22 per cent had been symptomatic less than one year. Among the various subgroups of admissions, only those with combined perforation and hemorrhage departed from this general pattern, 88 per cent of these having been symptomatic for less than five years and 42 per cent for less than one year. As will be discussed herein, this correlates with the relatively recent onset of the severe associated diseases commonly afflicting this group.

Site of Ulcer. Among the multiple entities

the ulcer sites were distributed as follows: duodenum, sixty-two; stomach, ten; pylorus, eight; both stomach and duodenum, four; and marginal ulcer, five. In addition to the four cases in which both the stomach and duodenum were involved, three patients had multiple duodenal ulcers and six had a single large ulcer involving both anterior and posterior duodenal walls, making a total of thirteen (15 per cent) having ulcer disease so extensive as to involve more than a single site.

Mortality. The death rate in the multiple entity group was four times as great as among those patients having only a single complication (Table 1), there being fifteen deaths (17 per cent of admissions) in the multiple entity group and thirty-six deaths (4 per cent of admissions) in the single entity group.

ASSOCIATED DISEASE

A large number of deaths in the multiple entity group resulted not from a catastrophe of peptic ulcer but from some serious unrelated disease, the ulcer diathesis frequently remaining a side issue in spite of its gravity. The frequency of unrelated malignancy appeared much higher than could be accounted for even on the basis of the advanced age of this group of patients.

There have been numerous reports of the association of peptic ulcer with disease of distant sites, the most famous being that of Curling in 1842, describing acute duodenal ulcerations following burns, and that of Cushing [2], presenting three instances of death from perforated peptic ulcer following craniotomy for cerebellar tumor.

Of the eighty-two patients with multiple entities (eighty-nine admissions) in the present study, twenty-one (26 per cent) had evidence of severe, unrelated disease. (Table III.) Eleven (13 per cent) had malignant tumors, of which five were bronchogenic carcinoma. Five of the fifteen deaths of patients with multiple entities were due, not to the effects of peptic ulcer but to the associated disease, four resulting from vascular disease and one from tumor. Another four of these fifteen deaths occurred in the presence of an advanced malignancy.

Dorn and Cutler [3] plotted the incidence of all types of malignancy in the general population of the United States against age. Their figure at age fifty-seven (the average age of the multiple entity group) was 750 per 100,000 population (0.75 per cent). Granting the dangers of comparing two such dissimilar groups, the 13 per cent frequency of malignant tumors within the multiple entity group is nevertheless seen to exceed this figure by almost seventeen times, a remarkable increase. No such marked association of other diseases with the complications of peptic ulcer appears in the literature.

TABLE III
ASSOCIATED DISEASES OCCURRING IN EIGHTY-TWO PATIENTS WITH MULTIPLE SIMULTANEOUS COMPLICATIONS OF PEPTIC ULCER

Associated Disease	No. of Patients
Malignant tumor (11 cases):	
Bronchogenic carcinoma	5
Carcinoma of pancreas	2
Lymphogenous leukemia	1
Lymphoepithelioma, pharynx	1
Mixed tumor of parotid	1
Metastatic melanoma	1
Severe cardiovascular disease (4 cases):	
Coronary occlusion	3
Congestive heart failure	1
Endocrine abnormalities (4 cases):	
Primary hyperparathyroidism	1
Islet cell adenoma of pancreas	1
Adrenocortical hyperplasia	1
Osteoarthritis (steroid therapy)	1
Miscellaneous (2 cases):	
Subdural hematoma	1
Active pulmonary tuberculosis	1
Total	21

By far the most severely afflicted patients were those with combined perforation and hemorrhage, seven (58 per cent) of these also having an associated disease. Among the remaining subgroups, the frequency of associated disease was: obstruction and perforation, 20 per cent; triple entity (perforation, hemorrhage, obstruction), 20 per cent; and obstruction and hemorrhage, 19 per cent.

In most cases, the history of ulcer considerably antedated that of the associated disease. The associated disease would therefore seem to exacerbate rather than initiate the peptic ulcer tendency.

The main significance of these findings is that they place an obligation upon the physician to make a thorough search for hidden, unrelated disease, especially tumor, in all patients suffering combined complications of peptic

ulcer. Of great interest was the fact that in fifteen cases (17 per cent of the multiple entity admissions) the associated disease had not been diagnosed prior to admission, and that in five of these, the early stage of the associated lesion and the paucity of its clinical signs resulted in a failure of diagnosis until long afterwards.

The Triple Combination. Combined perforation, hemorrhage and obstruction from peptic ulcer would seem to be exceedingly rare, there being only five reported cases. The first was that of Finsterer [*5*] in 1931, who performed plication and gastroenterostomy for a perforated, obstructed duodenal ulcer which had recently bled massively. The patient died of peritonitis. Since the remaining four instances [*1,8–10*] were reported within the past ten years, it is likely that this combination is not as rare as it seems. In the present study, no fewer than seven subjects were found, of whom two were private patients not included in the statistical analysis. Three of these cases are reported herein.

CASE REPORTS

Case 171 was that of a seventy year old white man who was admitted to The New York Hospital for the first time in 1946, with the chief complaint of severe abdominal pain of three hours' duration. Symptoms of ulcer had been present for three years. Examination revealed a rigid, diffusely tender abdomen, and a diagnosis of a perforated peptic ulcer was made. At laparotomy, a perforated prepyloric ulcer was found and sutured. A large mass proximal to the perforation was thought to be a gastric carcinoma although biopsy disclosed only chronic gastritis.

Postoperatively, the patient progressed well until the eleventh day when he began to have melena, followed by a drop in the hemoglobin value to 7.5 gm./100 cc. and requiring the transfusion of 1,000 cc. of whole blood. On the twentieth postoperative day, gastrointestinal series showed pyloric obstruction and a distended, fluid-filled stomach from which large amounts of coffee ground aspirate were obtained. Two days later, he suffered a myocardial infarction and remained in critical condition for the following week, requiring repeated transfusions because of the anemia.

On the fifty-seventh postoperative day, an x-ray film of the chest disclosed bilateral pulmonary infiltrates believed to represent metastases from a gastric carcinoma. Because of this, it was thought that no further surgery was indicated and the patient was discharged.

A gastrointestinal series one year later revealed no evidence of gastric disease, and an x-ray film of the chest showed bilateral, far advanced pulmonary tuberculosis, confirmed by sputum culture. He was referred to a municipal hospital for the treatment of the tuberculosis and during this hospitalization underwent gastric resection for further complications of the peptic ulcer. He died of far advanced pulmonary tuberculosis four years later.

The case just described is one of several cases discovered in this study in which a serious pulmonary disease presented for the first time during treatment for a severely complicated peptic ulcer.

Another patient (private case not included in statistical series), a white man, aged fifty-seven, was admitted for the first time in 1952, with a chief complaint of coffee ground vomiting of twenty-four hours' duration. He gave an eighteen-year history of ulcer and had had a marked increase in epigastric pain for the preceding two months. Examination revealed a thin, dehydrated white man in no great distress. Aspiration of the stomach produced 450 cc. of clear gastric contents.

During the following week, he continued to show severe pyloric obstruction. On the seventh hospital day, he was awakened at 5 A.M. by an excruciating abdominal pain. Examination disclosed a rigid, diffusely tender abdomen, and at operation, a perforated ulcer of the first portion of the duodenum was found and closed. Postoperatively, the persistent pyloric obstruction caused a severe electrolyte imbalance and the patient became confused and disoriented. On the seventh day, a wound dehiscence was closed under general anesthesia. On the following day, a massive bright red hematemesis occurred and the patient immediately went into shock. In spite of the administration of 4,000 cc. of whole blood, his condition never stabilized and he died in shock nine hours later. At autopsy, 1,500 cc. of clotted red blood were found in the enormously dilated stomach. A large posterior pyloric ulcer was found. So great was the dilatation of the stomach that its weight had pulled the duodenum inferiorly and twisted the margins of the posterior ulcer anteriorly, thus causing the previous perforation.

Practically no survivals are recorded following combined perforation and massive hemorrhage from peptic ulcer. Such a combination is usually caused by either a very large single ulcer involving both anterior and posterior duodenal walls or by multiple ulcers in both the stomach and the duodenum. In either case, the prospect for spontaneous cessation of massive hemorrhage is not good. This patient's condition was so desperate that immediate

gastric resection, even under local anesthesia, would probably not have been tolerated. Yet such measures should be considered in all who show such a combination. In the face of the history of marked pyloric obstruction prior to perforation, a concomitant gastroenterostomy would seem to have been indicated as a possible means of forestalling the combined obstruction and massive hemorrhage in the postoperative period. The mechanism by which the greatly dilated stomach twisted the posterior duodenal ulcer anteriorly in such a way as to cause a free perforation has never before been reported.

A third case (private case not included in statistical series) was that of a seventeen year old white boy admitted for the first time in 1954 with a history of severe epigastric pain, coffee ground emesis, and melena for one week. Since the age of eight, he had had periodic episodes of gnawing epigastric pain and vomiting. Examination revealed a healthy appearing youth with moderate, high epigastric tenderness.

For the first three days in the hospital, large amounts of coffee ground material were aspirated from the stomach, and because of a fall in the hematocrit, a single transfusion was administered. Thereafter, the bleeding appeared to have stopped but he continued to have large amounts of guaiac-negative aspirate. On the tenth day, he had a sudden abdominal pain which caused him to cry out and double up. At this time, the abdomen was rigid and diffusely tender. At operation, an anterior duodenal ulcer with perforation was found with much induration of the surrounding duodenal wall. Gastroenterostomy and transabdominal vagotomy were performed in addition to plication. The postoperative course was smooth and he was discharged in good condition two weeks later. Three and a half years later, he had gained 20 pounds and was free of ulcer symptoms. Gastrointestinal series showed a well functioning stoma and no marginal ulcer.

TREATMENT

Perforation-Hemorrhage Group. Much has been written about the treatment of these highly dramatic cases. Finsterer [*5*] reported three gastric resections for combined perforation and massive hemorrhage with one survival. Gordon-Taylor [*6,7*] divided them into three groups according to whether the hemorrhage followed, preceded or coincided with the perforation. In five patients of the last group, all apparently with massive hemorrhage, he employed primary gastric resection with 100 per cent survival. Of eight other patients in whom the entities were not simultaneous but in close succession upon one another, all died although resection was tried in five. He thus believed that the timing of the events was of great significance. Ives [*11*] thought that immediate gastrectomy for hemorrhage following perforation might offer the only chance for survival.

In this study, seventeen cases of perforation and hemorrhage (including the five triple entities) were analyzed as a unit. Seven (41 per cent) of these patients died in the hospital, including all five of those having massive hemorrhage. Among the twelve patients with non-massive hemorrhage, there were only two (17 per cent) deaths, emphasizing the prognostic importance of the severity of the bleeding. That it was not insignificant even in the non-massive group, however, is shown by the fact that these patients required an average transfusion of 2,600 cc. There were two cases in which fatal, massive hemorrhage following plication occurred from unsuspected high gastric ulcers.

The inadequacy of plication alone, without further definitive surgery, in the treatment of the perforation and hemorrhage group, is illustrated by the fact that only one of the eight patients having plication alone had a satisfactory long term result.

Four conclusions concerning the treatment of the perforation and hemorrhage group can be drawn: (1) When massive hemorrhage closely follows the plication of a perforation, the patient's precarious general condition may preclude any surgery, but emergency gastrectomy usually offers the only hope of survival. (2) A search for multiple ulcers in the stomach and duodenum should be made at the time of every plication, and primary gastric resection strongly considered if they are found. (3) In the face of pyloric obstruction found at the time of plication, the performance of a gastroenterostomy may obviate not only postoperative obstruction but fatal massive hemorrhage. (4) A patient surviving combined hemorrhage and perforation should be rapidly prepared for gastric resection because of the universally poor results following simple suture alone.

Perforation-Obstruction Group. Surgical closure was performed in these fifteen patients, of whom four died in the hospital. Two of the remainder required subsequent gastroenterostomy for pyloric obstruction during the same

admission; both of these patients were well eight years later. (Both were white men, aged thirty-one.) Moore and Hendricks [*14*] found that gastroenterostomy for obstruction present at the time of plication was not attended by a higher mortality in good risk patients, and that subsequent operation was unnecessary in a significant number of these. These two cases seem to confirm this. Of the remaining nine patients who had no other procedure than plication performed during this admission, seven required further surgery for ulcer on subsequent admissions, one was lost to follow-up, and one was treated for hemorrhage two months later. Thus, the results following plication alone were nearly 100 per cent unsatisfactory and may be compared with those of Moore [*13*] who found failure in 46 per cent of one series and 66 per cent of another series of patients having only the single entity of perforation. It would thus seem that perforation combined with obstruction is a positive indication of intractability, requiring early, definitive surgical treatment of the ulcer.

Hemorrhage-Obstruction Group. Of the fifty-seven patients in this group, forty-seven (82 per cent) were operated upon during the same admission, thirty-three undergoing gastric resection. As a whole, the group presented no unique management problem.

Triple-Combination Group (Perforation, Hemorrhage, Obstruction). The special problems of treatment of this small group are discussed in the previous case reports. It is interesting that the mortality in this group was less than among those with only perforation and hemorrhage. (Table 1.)

SUMMARY

A study of 969 cases of perforation, hemorrhage, or obstruction of peptic ulcer discloses that nearly ten per cent of these patients have more than one of these entities at the same time, and that such combinations produce a mortality four times as great as cases with only one such complication.

There was a strong association of severe, unrelated diseases, especially malignant tumors, in the multiple entity group. Over a fourth of the patients in this group were thus affected. That these associated lesions are often in an early and previously undiagnosed state at the time of the admission for the combined complications suggests that they may serve to exacerbate an existing ulcer tendency and that a severely complicated peptic ulcer may indeed be an early warning signal of their presence. A vigorous work-up, especially for active pulmonary disease, is indicated in every patient surviving combined complications of peptic ulcer.

The triple combination of perforation, hemorrhage and obstruction is much more common than previously believed, having appeared in five instances in this study.

The high mortality of the perforation and hemorrhage combination when the hemorrhage is massive is again confirmed. Its management is largely preventive and requires a search for multiple ulcers at the time of plication for perforation. If these are found, primary subtotal gastrectomy should be strongly considered. Simple gastroenterostomy, gastroenterostomy with vagotomy, or primary gastric resection should be performed for an obstructed perforated ulcer. Such an ulcer usually involves both the anterior and posterior pyloric walls and makes more likely the occurrence of a massive postoperative hemorrhage as well as dehydration and electrolyte imbalance from pyloric obstruction, unless the additional procedure is performed. When actually confronted with a massive hemorrhage occurring near the time of perforation, the surgeon may be powerless because of the desperate general condition of the patient. However, vigorous blood replacement coupled with immediate gastric resection usually offers the only hope for survival.

The occurrence of multiple combined complications is a positive indication of advanced, intractable ulcer disease requiring definitive surgical treatment, usually gastric resection, at the earliest possible moment.

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"Surgeons emerged as a professional group, whose aim was not magic but true surgery, in Babylon, about 2000 B.C. As a professional class they were subject to regulations and penalties under the code of laws known as the Code of Hammurabi, which was inscribed on a stone discovered at the beginning of this century, and if they are a somewhat startlingly direct approach to the problem of regulating medical practice, these provisions of the Code were obviously written with good intent:

"'If a physician operate on a man for a severe wound with a bronze lancet and cause the man's death; or open an abscess of a man with a bronze lancet and destroy the man's eye, they shall cut off his fingers.'

"'If a physician operate on a slave of a freeman with a bronze lancet and cause his death, he shall restore a slave of equal value.'" (From: Young, A. Scalpel: Men Who Made Surgery, p. 5. New York, 1956. Random House.)

The Prophylaxis and Treatment of Postpartum and Postoperative Ileus with Pantothenyl Alcohol

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THE scientific background for subsequent clinical investigation of the value of pantothenyl alcohol in preventing and treating enteric atony and ileus was furnished by Lipmann and co-workers [1] in 1950. They showed that pantothenic acid forms part of coenzyme A necessary for the acetylation of choline, in order to form acetylcholine, which is the neurohumoral agent required for intestinal activity, both motor and secretory. In experimentally induced pantothenic acid deficiency in humans, Bean, Hodges and Daum [2] found a fall in acetylcholine production, with a resulting tendency toward enteric atomy. In 1955 Orecchia [3] suggested that a lack of pantothenic acid in surgical patients, as well as in infection and circulatory disturbance, contributes toward intestinal ileus. Biochemical studies by Lynch, Spurgeon and Worton [4] have further shown that in various experimental stress situations the blood and tissue levels of pantothenic acid are altered.

PHARMACOLOGY

It has long been established that acetylcholine is the transmitted substance at the synapse and postganglionic fiber endings of the parasympathetic nervous system which is necessary for the maintenance of normal peristalsis. Thus it is clear that pantothenic acid is a necessary precursor for the satisfactory functioning of the parasympathetic nervous system in the intestinal tract in order to maintain normal physiologic motility. Pantothenic acid combines with some protein moiety to form coenzyme A. Coenzyme A produces acetylcholine from acetate and choline. Acetylcholine is the necessary neurohumoral transmitter for parasympathetic activity and thus is essential for maintaining intestinal peristalsis. Cholinesterase breaks up acetylcholine very quickly after it is formed. This prevents an accumulation of acetylcholine and an excess of intestinal activity. Many drugs will inhibit cholinesterase and thus allow an accumulation of acetylcholine. Some of these drugs, such as neostigmine, are eserine derivatives. Such drugs tend to allow so much acetylcholine to accumulate that there may be resulting cramping, hypermotility and diarrhea. On the other hand, promotion of coenzyme A formation will contribute to a normal production of acetylcholine which then, under ordinary conditions, will be destroyed quickly after its formation so as to maintain normal intestinal activity without too great an increase.

Pantothenyl alcohol does not simulate acetylcholine in action and does not interfere with cholinesterase, the physiologic governor that protects against acetylcholine excesses. Thus it may be expected of pantothenyl alcohol that side effects such as abdominal pain, nausea, vomiting, hypotension and profuse sweating may be avoided.

Experimentally it has been shown from intestinal recordings by a balloon inserted into the ileum of a normal rabbit that the intravenous infusion of pantothenyl alcohol causes no change in the usual pattern of peristaltic contractions while infusion with choline derivatives causes marked hyperperistaltic reaction.

PREVIOUS CLINICAL STUDIES

Clinical study was begun by Jacques [5] on the basis of observation in rats that deficiency of pantothenic acid produces interruption of peristaltic activity. Jacques obtained marked success in treating paralytic ileus by using injections of calcium pantothenate.

In 1953 Felten [6] used pantothenyl alcohol in large doses in fifty cases of complete retention of flatus following general surgical or gynecological operations. He gave 500 mg. intramuscularly and noted rapid effect in almost all cases, the flatus being expelled in twenty to sixty minutes and the first defecation most frequently occurring in twenty-four hours.

In 1955 Sclausero [7] gave pantothenyl alcohol in thirty-four cases prophylactically after surgery, using 500 mg. intramuscularly twenty-four hours postoperatively and another 500 mg. intramuscularly thirty-six hours postoperatively. Only six patients required other aid. He further treated ninety-two cases that showed delay in resumption of peristalsis postoperatively. Satisfactory results were obtained with one dose (500 mg. intramuscularly) in thirty cases, with two doses in twenty-nine patients, and with three doses or more in twenty-three cases. In the remaining ten cases peristalsis occurred no more quickly than would otherwise be expected.

Lang and Ernst [9] used pantothenyl alcohol in the treatment of more than 200 cases of paralytic ileus following diversified surgical procedures. They are convinced that there are no undesirable reactions from the drug and now the drug is used routinely in all forms of ileus even following intestinal anastomosis.

Warlitz [9] studied the effects of pantothenyl alcohol in 100 cases of postoperative intestinal atony. He concluded that the drug exerts a favorable reaction in restoring intestinal motility in a short period of time and observed no undesirable side effects at all.

In the United States, Kareha, deQuevedo, Tighe and Kehrli [10] were among the first to study the use of pantothenyl alcohol in the prevention and treatment of ileus in patients after operation. They found that in abdominal surgery where intestinal tubes are standard procedure, the tubes may be removed two to five days sooner; in cases in which tubes are not standard procedure their use is practically eliminated, bowel activity returning usually in twenty-four to thirty-six hours and the abdomen remaining flat and flatus passing within twelve to thirty-six hours. They found that the patients were much more comfortable and that no hyperperistalsis or cramping was noted. They were able to relieve or prevent postoperative abdominal distention in more than 90 per cent of their cases.

PRESENT STUDY

This present report includes 130 patients who received pantothenyl alcohol for either the prevention or treatment of ileus. The pantothenyl alcohol* corresponds to, and is transformed into, pantothenyl acid. The high solubility in this form permits effective dosage in a concentrated intramuscular injection. The standard dose was 500 mg. (2 cc.) immediately postoperatively or postpartum. This dosage was repeated in two and twelve hours.

Material

The 130 patients were classified into five groups. Group I consisted of forty-two obstetrical cases in which delivery was made with or without the use of forceps. Group II included seventeen cases of cesarean section. Group III included three cases of postcesarean distention. Group IV consisted of thirty-two cases of hysterectomy. Group V was a miscellaneous group of thirty-six cases including intestinal surgery with resections and anastomoses.

Results

GROUP I. In these cases spontaneous passage of gas per rectum usually occurred well within twelve to fourteen hours. In only one case was postpartum distention sufficient to be a problem. The patients receiving the drug did not complain of cramping or any more than normal postpartum abdominal pain that could be accounted for on the basis of uterine involution. No more analgesics were used in this group than in the routine postpartum case. Postpartum catheterization was not necessary in this group.

GROUP II. In sixteen cases the patients passed gas per rectum spontaneously within forty-eight hours. In the remaining case there was marked distention on the third postopera-

* Clinical supplies of this material under the trade name ilopan were furnished by The Warren-Teed Products Co., whose courtesy is herewith gratefully acknowledged.

tive day. Pantothenyl alcohol was repeated for three further dosages (500 mg. each time), with resultant relief of distention and passage of flatus within twenty-four hours of the initiation of the second series. In almost all cases the requirements for catheterization of the urinary bladder were markedly diminished to absent.

GROUP III. There was marked relief of the distention within twenty-four hours. In the case of one author (S. S.) gas and flatus were passed within one hour of the administration of the drug and the distention was visibly relieved within that time. The patient experienced no cramping or other undesirable side reactions and felt enormously improved symptomatically.

GROUP IV. Twenty-eight patients passed gas spontaneously by the third postoperative day. All had enemas on the third postoperative day, either early or late. Of the four patients who did not pass flatus, only two had sufficient distention to constitute a problem. In one of these cases a Levin tube was passed on the second postoperative day and removed fourteen hours later after a successful enema. In the remaining case a poor result with an enema on the third postoperative day necessitated the use of a Cantor tube which remained in place for three days for marked distention although flatus was passed.

GROUP V. In this group pantothenyl alcohol was used for treatment in cases in which moderate or marked distention or ileus developed after major surgery. In many of these cases intestinal tubes (Miller-Abbott, Levin or Cantor) were used. All patients received usual supportive treatment; enemas, rectal tubes, etc. Pantothenyl alcohol in the dose of 500 to 4,000 mg. was used per patient from the fourth to the seventh day postoperatively. In some cases the results were excellent, with rapid return of normal peristalsis and marked relief of distention and symptoms. In some cases the return to normal was slow and unimpressive in spite of repeated courses of treatment. The actual results were not broken down further because of the vast differences and underlying pathologic condition in this group; however, no ill effects from the use of pantothenyl alcohol were observed.

The rapid return of normal intestinal activity in these patients after the use of the pantothenyl alcohol preparation contrasts significantly with our experience with similar patients followed previously, when the pantothenyl alcohol was not available. It was usual then for this kind of patient to have several days of distention, atony and often ileus, with much discomfort, before normal bowel action could be expected. During this period much time and effort would be devoted to dietary control and other measures in order to reduce discomfort and distention. With the use of the pantothenyl alcohol preparation this time of postoperative discomfort is practically abolished and the patients are relatively free from abdominal distress after the same type of operative procedures.

Side Effects

In all cases the drug was well tolerated. There was no instance of increase in peristalsis and no difficulties in those patients who had intestinal anastomoses. No untoward allergic reactions or other idiosyncrasies were noted. None of the patients exhibited abdominal pain, nausea, vomiting or hypotension associated with the administration of pantothenyl alcohol.

SUMMARY

1. Pantothenyl alcohol forms part of coenzyme A that is required for normal function of the parasympathetic system (acetylation of choline) and thus is necessary for normal peristalsis.

2. Surgical stress, circulatory disturbances and infection may lower the level of pantothenic acid in the body, thus producing a background for ileus.

3. Pantothenic acid does not produce cramping or hyperperistalsis, as is the case with cholinesterase inhibitors such as eserine derivatives.

4. A brief review of the foreign investigations and the study by the Hahnemann group, as well as the current series from the Metropolitan Medical Center, is presented.

5. We have found in our study (130 cases) at the Metropolitan Medical Center that pantothenyl alcohol (Ilopan) is a frequently useful drug in the prevention of postoperative ileus and in its treatment.

6. No ill effects from the drug were noted.

7. In our series postoperative urinary retention was greatly reduced. The catheterization requirements were substantially diminished

and this "fringe benefit" contributed to the lessening of patient discomfort and postoperative urinary tract infection. Although more investigative clinical work needs to be done on this facet of the problem for definitive evaluation, we may suggest that if postoperative or postpartum urinary retention is anticipated or seen, pantothenyl alcohol may be administered safely as a routine without fear of any untoward reactions from the drug.

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"It was at Avignon that Guy de Chauliac saw and suffered from the Black Death. This great pestilence first reached Europe in the autumn of A.D. 1347, after having raged in the Far East for over three years. In China thirteen millions of people died; India was almost depopulated; Mesopotamia, Syria, and Armenia were ravaged. Slowly, the pestilence spread westwards. Near Constantinople the city of Caffa was besieged by Tartars. The Black Death seized the invading army, and thousands died each day. Bacterial warfare was born then as the survivors catapulted into the city from the engines of war the putrefying bodies of their friends. Within the space of days the last of the besieged had died as horribly as had the last of the besiegers." (From: Graham, H. Surgeons All, p. 110. New York, 1957. Philosophical Library, Inc.)

The Eosinophil and Gastrointestinal Carcinoma

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EOSINOPHILS are frequently observed in varying numbers in and about neoplastic tissue. Many patients with carcinoma involving a viscus show some degree of increase in eosinophilic leukocytes in the peripheral blood. This study and review of the literature constitutes an evaluation of the significance and importance of these findings.

In reviewing the literature, many authors have reported either eosinophilia of the peripheral blood associated with malignancy [*3,4,7,12,13,15,17,19,22–26,29,31,33,35,38,40–42,44*] or eosinophilic infiltration of the tumor tissue [*2,9–11,19,20(a),20(b),21,25,27,28,30,32,36,37*].

In 1893, Reinbach [*33*] was the first to report a case of blood eosinophilia (48 per cent) in carcinoma of the neck. Since then similar cases have been described sporadically in patients with carcinoma of the cervix [*35–38*], penis [*32*], gastrointestinal tract [*4,42*], lung [*19*], liver [*22*], and sarcoma [*3,26,44*]. In 1946, Isaacson and Raport [*17*] collected thirty-four such cases including fifteen of their own and concluded that eosinophilia, when it occurs in patients with malignant tumors and when other causes can be ruled out, is indicative of dissemination and consequently signifies a poor prognosis. Later Grewe and Schlitter [*12,13*], Linke [*21*], Majumdar and Zahn [*23*], Murray [*24*], and Querido [*31*] reported similar cases and agreed with Isaacson. In 1896, Przewoski [*28*] first described a local eosinophilic infiltration in carcinoma. Eleven years later, Kappis [*19*] noted both blood eosinophilia (33 to 35 per cent eosinophilia) and eosinophilic infiltration in carcinoma of lung. In 1922, Lahm [*20(a),20(b)*] was apparently the first to mention that malignant tumors with eosinophilic infiltration had a better prognosis than those without eosinophilic infiltration. Immediately after this Schoch [*36,37*], Pavlovsky and Widakowich [*27*], Fluhmann [*10*], and Goforth and Snoke [*11*] emphasized this same point. Nothing more was written about these points until Fischer [*9*] in 1952 stated that eosinophilic infiltration in tumor tissue is usually associated with a poor prognosis. In 1956 Podhragyai [*30*] studied 1,087 cases of carcinoma of the skin and seventy intestinal, breast and uterine carcinomas and concluded that there is no relation between prognosis and the degree of eosinophilic infiltration in tumor or eosinophil percentage in blood.

Because there are controversial opinions on this subject, I decided to study 129 gastrointestinal carcinomas and attempt to define the significance of eosinophilic infiltration of tumor tissue and peripheral blood eosinophilia. This paper deals with the results of this study and a review of the pertinent literature.

MATERIAL AND METHOD

Two hundred fifteen cases of adenocarcinoma of the colon and stomach were collected from the pathology files of Morristown Memorial Hospital from 1935 to 1956 inclusive and examined microscopically. The degree of eosinophilic infiltration was evaluated and recorded as follows: eosinophils less than five per high power field (× 500, wide field) classified as "−"; five to twenty eosinophils, "+"; twenty to fifty eosinophils, "++"; more than fifty eosinophils, "+++." The tumors were also classified according to the methods of Broders [*1*] and Dukes [*1*] for comparison. Follow-up studies were obtained on 129 cases and clinical data have been reviewed on these. All of the patients included in this study had had definitive surgery performed. The patients on

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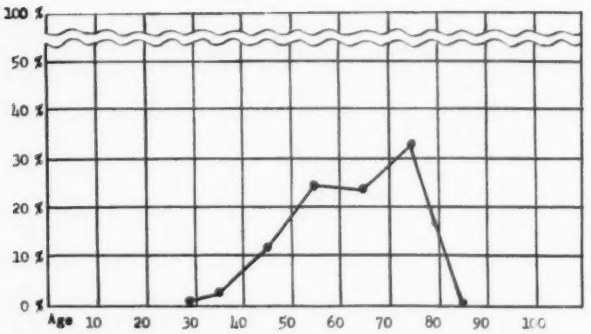

FIG. 1. Age incidence of 129 patients with gastrointestinal carcinoma.

whom only biopsy was performed have been excluded from this study.

The microscopic sections were reviewed by two other pathologists (twenty sample cases) for intensity of the eosinophilic infiltration and they essentially agreed with my classification. The eosinophilic infiltrate was usually in the desmoplastic tissue and only rarely in the carcinoma itself. The degree of infiltration was found to have no discernible relation to the amount of desmoplastic reaction. There were almost always other inflammatory cells seen; these were lymphocytes, plasma cells and segmented neutrophils. A certain amount of necrosis of tumor tissue was found in all of these neoplasms but there was no appreciable relation between eosinophilic infiltration and the amount of necrosis. The eosinophil count was taken in the desmoplastic area in which no necrosis was present.

RESULTS AND COMMENTS

The patients' ages ranged from twenty-nine to eighty-six years and 80 per cent were more than fifty years old. (Fig. 1.) The ratio of men to women was about 1:1. There were twenty-one adenocarcinomas of the stomach and 108 adenocarcinomas of the colon (including rectum). The peripheral white blood cell counts ranged from 5,150 to 23,000 per cu. mm. with 0 to 13 per cent eosinophils. There were nine patients who had more than 6 per cent eosinophils. (Table 1.) Of these, two patients died postoperatively (Cases 3 and 8) and two died (Cases 6 and 7) within a year. Three patients died in twelve to sixteen months (Cases 1, 2 and 9) and two lived for two years (Cases 4 and 5). As Table 1 shows, tissue eosinophilia and peripheral blood eosinophilia sometimes parallel each other but there were sixteen patients who had +++ eosinophilic infiltration without eosinophilia being found. (Hereafter eosinophilia applies to peripheral blood eosinophils over 6 per cent and eosinophilic infiltration applies to local tissue eosinophilia in tumors.) However, of the nine patients in

TABLE 1

EOSINOPHILIA IN PERIPHERAL BLOOD ASSOCIATED WITH GASTROINTESTINAL CARCINOMAS

Case No.	Age and Sex	Broders' Classification	Dukes' Classification	Eosinophilic Infiltration in Tumors	White Blood Count (per cu. mm.)	Eosinophilia in Blood (Per cent)	Length of Survival (mo.)	Autopsy	Autopsy Findings
1	65, M	II	B	−	7,600	7	13	−	Metastasis in small intestine*
2	68, M	II	C	++	12,000	10	12	+	Metastasis in liver, lung, kidney
3	66, M	II	B	+	8,600	13	¼	+	Metastasis in lung
4	61, F	II	C	++	10,800	12	24	+	Metastasis in lung, liver, ovary and pancreas
5	36, M	II	C	+++	7,200	8	24	+	Diffuse peritonitis (operation for lysis)
6	82, F	II	B	++	6,400	8	8	−	Metastasis in skin and intestine*
7	78, M	II	C	++	10,500	10	4	+	Metastasis in liver, lung, pancreas
8	66, F	III	C	++	10,200	8	½	−	Metastasis in omentum*
9	43, M	III	B	+	11,300	8	16	+	Metastasis in liver and lung

* Clinical findings.

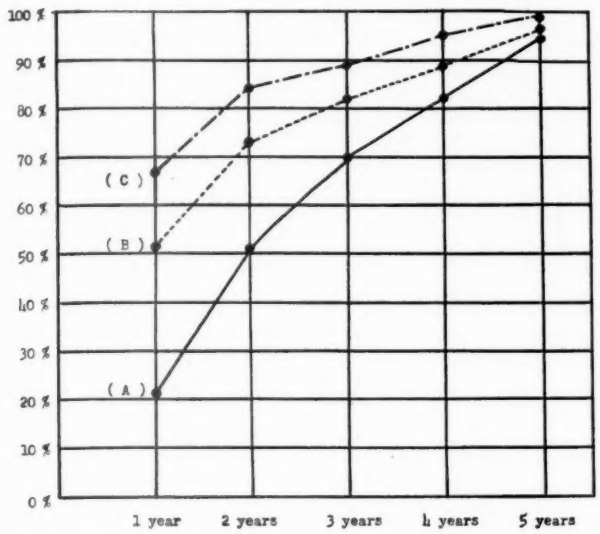

FIG. 2. Dukes' classification, mortality of 129 patients with gastrointestinal carcinoma.

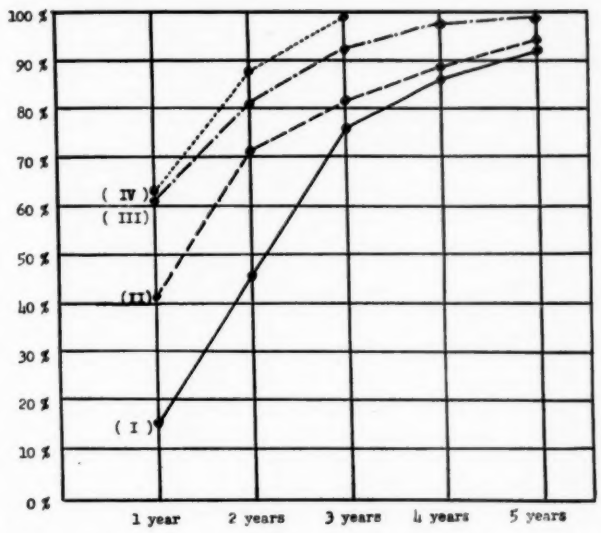

FIG. 3. Broders' classification, mortality of 129 patients with gastrointestinal carcinoma.

this series who had eosinophilia, eight had a certain amount of eosinophilic infiltration. The two postoperative deaths are considered to be due to surgical complications and of course no conclusions related to either eosinophilia or eosinophilic infiltration can be reached. Five patients (Cases 2, 4, 5, 7 and 8) had evidence of metastasis at the time of surgery and in four patients (Cases 1, 3, 6 and 9) metastatic lesions subsequently developed. One patient (Case 5) died following surgery for lysis of abdominal adhesions. No neoplasm was found at this second operation, performed two years after the first, even though regional lymph node metastases were found in the original surgical specimen. The findings in these cases agree with Isaacson's [17] opinion that blood eosinophilia usually means the presence of metastases.

There were thirty-six cases in Dukes' classification A, forty-two cases in group B, and 51 cases in group C. At the end of the first year group A (Dukes) showed 22.4 per cent mortality, group B, showed 52.9 per cent, group C showed 66.5 per cent; the mortality increased as the years passed as shown in Figure 2. Among 129 cases, nineteen cases belonged to Broders' classification grade I, seventy-eight cases to grade II, twenty-four cases to grade III, and eight cases to grade IV. At the end of the first year those patients in grade I showed 15.6 per cent mortality; grade II, 42.0 per cent; grade III, 61.5 per cent; grade IV, 62.5 per cent; and the following year the mortality rate had greatly increased as shown in Figure 3. The study of eosinophilic infiltration in tumor tissue gave results as follows: thirty-nine cases fell into group −; forty-seven cases, group +; twenty-eight cases, group ++; fifteen cases, group +++. Group − showed 60.0 per cent mortality at the end of the first year and group +, 48.3 per cent; group ++, 36.0 per cent; group +++, 19.8 per cent. It is noted that the more intense the eosinophilic infiltration, the better the prognosis; this is shown in Figure 4. In comparing Figures 2, 3

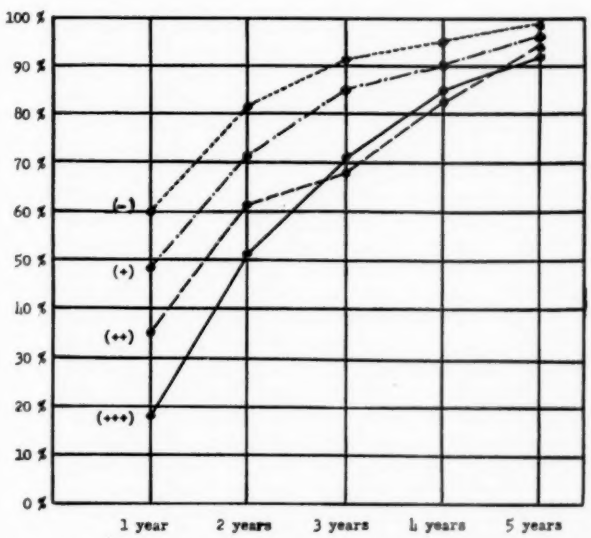

FIG. 4. Classification according to the degree of eosinophilic infiltration, mortality of 129 patients with gastrointestinal carcinoma.

TABLE II
PATIENTS CLASSIFIED IN DUKES' A AND +++ EOSINOPHILIC INFILTRATION (EIGHT CASES)

Case No.	Age and Sex	Broders' Classification	Dukes' Classification	Eosinophilic Infiltration in Tumors	Follow-up
1	60, M	II	A	+++	Alive, 5 yr.
2	66, F	II	A	+++	Died, 4 yr. postoperatively
3	53, F	I	A	+++	Alive, 3 yr.
4	70, M	I	A	+++	Alive, 3 yr.
5	52, M	I	A	+++	Alive, 2 yr.
6	58, M	II	A	+++	Alive, 5 yr.
7	71, F	II	A	+++	Alive, 3 yr.
8	86, M	I	A	+++	Died, 2 yr. postoperatively

and 4 there is similar prognostic difference at the end of each year.

The patient who belonged to Dukes' classification A, Broders' grade I, and +++ eosinophilic infiltration had a better prognosis according to this study. I found eight such cases as shown in Table II. The oldest patient died two years postoperatively and another died four years after surgery; the remaining six are living and apparently free of disease a varying number of years.

Nineteen sternal marrow specimens were available for study on the patients in this series. Ten of them showed no eosinophilia and nine showed slight-to-moderate eosinophilia. The patients who had tissue eosinophilia did not show any eosinophilic hyperplasia in marrow but those who had eosinophilia in the peripheral blood did show some degree of eosinophilia in their marrow.

It seems to be logical that eosinophilic infiltration in tumor tissue is merely a local reaction [*29*] and not necessarily associated with peripheral blood eosinophilia. Many authors [*9,12,13,15,17,19,22,23*] have considered it as an allergic response to necrotic tumor tissue. Weiss [*42*] injected tumor extracts into laboratory animals; he was not able to produce eosinophilia but only a slight leukocytosis. Battaglia [*2*] observed eosinophilic infiltration in tumors and believed some carcinomas produce more lactic acid whereas others produce less; he concluded that the more lactic acid, the more eosinophils. The function of the eosinophil is not well understood but it seems more probable that these cells are concerned in some way with combating histamine [*16*]. Speirs [*39*] stated that eosinophils are attracted to the site of antigen-antibody reaction, but antigenic material *per se* does not produce a systemic increase but rather a slight local accumulation of eosinophils. Also, he mentioned that eosinophils must be attracted there by some chemotactic substance, possibly a material released when antigen and antibody combine. Eosinophilia is seen in various conditions such as allergic disorders, pemphigus, dermatitis hypertiformis, pernicious anemia, benzol poisoning, Hodgkins disease [*43*] and parasitic diseases [*6*]. It has also been reported in cases of arsenic intoxication [*14*], chronic relapsing pancreatitis [*18*], endocardial fibrosis [*5*], Löffler's syndrome [*8*], pleural effusion associated with trauma, tuberculosis, pulmonary infarction, pneumonia [*34*] and in malignancy.

Sala's [*38*] and Isaacson's [*17*] cases showed marked eosinophilia with carcinoma of cervix and lung simulating aleukemic leukemia. According to Isaacson, 90 per cent of all reported patients with eosinophilia had evidence of metastases, and he found fifteen patients showing 10 to 32 per cent eosinophils in peripheral blood among 2,363 patients with malignancy. Stickney and Heck [*40*] reported that 5 per cent of 418 patients with malignancy showed 6 to 10 per cent of eosinophils and 1.3 per cent of the same group showed 10 to 20 per cent of eosinophils. In 1954 [*12*] Grewe reported, among 800 patients with malignancy, 197 showed more than 5 per cent eosinophils.

In my series there were nine patients (6.93 per cent of 129 cases) with eosinophilia and all of these had diffuse metastases. (Table I.) Podhragyai [*30*] states that thirteen patients showed eosinophilia and eosinophilic infiltration in tissue but seven of these had had radiation therapy.

Eosinophilia in patients with malignancy seems to be associated with poorer prognosis. Many authors agree on this and there is only one contrary opinion in the literature, that of Podhragyai [*30*].

In 1949 Querido [*31*] first suggested that eosinophilia be used in the differential diagnosis of neoplastic and non-neoplastic lesions. Murray [*24*] later made a study of eighteen carcinomas of lung, five of which had an x-ray picture resembling abscess of the lung. He found that all eighteen of these had an absolute eosinophil count of greater than 500 and he believed that this point may be helpful in

making a differential diagnosis between abscess of the lung and carcinoma.

Eosinophilic infiltration is seen in varying quantity in peptic ulcer, allergic inflammation [30], Löffler's syndrome [8], following radiation therapy and malignant tumor tissue. Schoch [37] studied 407 cases of carcinoma of cervix. Forty patients had eosinophilic infiltration and of these, 45 per cent had a five-year survival, whereas in the group without eosinophilic infiltration, only 10 per cent survived five years.

Pavlovsky [27] believed eosinophils have a protective action against invasion by carcinoma and Goforth and Snoke [11] feel strongly that the presence of eosinophilic infiltration is a good sign in carcinoma of the cervix and the greater the number the more favorable the prognosis. However, Fischer [9] believes that eosinophils in tumor tissue indicate a poor prognosis. Recently, Podhragyai [30] studied twenty-two intestinal, twenty-seven breast and twenty-one uterine carcinomas and found eosinophilic infiltration in the tumor tissue in 8.4 per cent; none of these had been radiated. He also studied 511 epidermoid carcinomas treated by x-ray following biopsy and he observed that 25 per cent of them showed eosinophilia in the peripheral blood. He concluded that one may consider blood and tissue eosinophilia as a general or local tissue reaction produced by protein derived from degeneration of tumor tissue. He does not believe this is related to prognosis.

Eosinophilic infiltration in carcinoma appears to be a very favorable finding as regards prognosis. I believe this thesis is substantiated in this study. Apparently the local eosinophilic response represents some sort of protective reaction. Eosinophilia with evidence of metastases was found in five patients at the time of surgery and subsequent metastases occurred in the remaining four in this study. It is possible that when the tumor undergoes metastasis the eosinophilic response becomes generalized and naturally the prognosis is poor. On the other hand, eosinophilic infiltration without eosinophilia suggests the disease is still localized and has a better prognosis.

In general, eosinophilic infiltration in tumor tissue is a good sign; however, the prognosis of a patient cannot be judged by this factor alone, because even though the patient might have +++ eosinophilic infiltration the tumor may have already metastasized. In attempting to evaluate the prognosis in patients with carcinoma, we should consider all the facts which may be pertinent.

SUMMARY AND CONCLUSIONS

One hundred twenty-nine gastrointestinal carcinomas have been studied and evaluated for eosinophilic infiltration. This study offers evidence that the more eosinophilic infiltration in carcinomas of the stomach and colon, the better the prognosis. This is compared with Broders' and Dukes' classifications and the results are very similar. The evidence also strongly suggests that an increase in blood eosinophils in patients with carcinoma makes the prognosis worse.

The literature is reviewed and the various opinions on the relation of prognosis, eosinophilic infiltration and blood eosinophilia are presented and discussed.

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Congenital Internal Hernia

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THE differential diagnosis of abdominal pain remains one of the most challenging problems confronting physicians. Although not a common lesion, internal hernia is a cause of abdominal pain which is difficult to diagnose. In an attempt to clarify the clinical picture and to determine whether this diagnosis can be established preoperatively I have reviewed the literature and the cases seen at this institution during the past five years. Eight cases of congenital internal hernia were seen during the past five years and of these, three were acutely obstructed and no further diagnosis made prior to surgery. Four of the remaining five were correctly diagnosed preoperatively by the radiologists.

ETIOLOGY

The etiology of internal hernia is varied but may generally be stated as congenital or acquired. Andrews [1] first noted that most fossal internal hernias are anomalies of rotation and development of the mid-gut which eventually becomes the jejunum, ileum, and right colon. Callander et al. [2], Johnson [5], and Zimmerman and Laufman [9] have studied the etiology of congenital internal hernias and believe that the hernias result from failures of development, rotation, and apposition. Internal incarceration can also be caused by congenital bands or defects without any developmental or rotational anomalies but these are probably not true hernias. The acquired hernias are most frequently seen following surgery with a few reported after trauma and inflammation. It is difficult to determine the exact nature of many of the acquired or postoperative hernias and therefore these have been omitted from this discussion except for the statement that practically all those seen were operated upon with the diagnosis of acute intestinal obstruction and the exact nature of the lesion has been of academic interest only since the indication for surgery was clear. Three of our patients had had previous surgery but we believe that the evidence clearly supports a diagnosis of congenital hernia apparently not noted at the previous surgery. All three had definite developmental or rotational anomalies noted at surgery when the diagnosis of internal hernia was established.

CASE SUMMARIES

Our experience is summarized in Table 1. None of the three paraduodenal hernias were acutely obstructed but all occurred in adults who had symptoms of recurrent crampy upper abdominal pain of one to three years' duration. This was usually worse after eating and all patients had vomited on occasion after eating. Two of the three patients had lost considerable weight. A clinical diagnosis of cholecystitis had been made in one instance. The Radiology Department was able to make the correct diagnosis by upper gastrointestinal barium study in all three cases.

There were three cases of congenital transmesocolic hernia, one presenting as acute intestinal obstruction. In the second case, a patient on whom previous pelvic surgery had been performed, there was incomplete rotation of the right colon. The third case was successfully diagnosed by x-ray examination.

Two cases of paracecal hernia presented as acute intestinal obstruction with symptoms of one and five days' duration and were successfully treated surgically.

COMMENTS

The literature on this subject is comprised largely of case reports and the largest individual series found was that of Mayo, Stalker and Miller [7] who reported thirty-nine cases with eighteen congenital and twenty-one acquired

FIG. 1A. Case II. A conglomeration of barium-filled jejunum is noted to the right of the duodenum indicating a right paraduodenal hernia. Jejunum is also absent from the left upper quadrant of the abdomen.

FIG. 1B. Case II. The lateral view shows the proximal jejunal loops located posterior and to the right of the duodenum.

postoperative hernias collected from 1910 to 1939. They report acute intestinal obstruction in nineteen patients and symptoms in a total of twenty-nine but do not differentiate primary from acquired hernias and do not give any mortality figures.

Zimmerman and Laufman [9] reported twelve cases of true congenital internal hernia found in a ten-year period at the Cook County Hospital. Surgery was performed in eight of the cases with an operative mortality of 37 per cent and an over-all mortality of 58 per cent. The largest collective series is that of Hansmann and Morton [4] who collected 467 cases and added

TABLE I

Case	Age	Year	Diagnosis	Radiologist's Diagnosis	Symptoms	Obstruction
I	61	1952	Right paraduodenal hernia	Internal hernia	Pain in right upper quadrant postprandial nausea and vomiting	No
II	47	1953	Right paraduodenal hernia	Internal hernia	Epigastric pain, 30 lb. weight loss	No
III	31	1955	Right paraduodenal hernia	Internal hernia	Postprandial cramps, 30 lb. weight loss	No
IV	60	1954	Transmesocolic hernia	"Chronic obstruction"	Diarrhea	No
V	48	1954	Transmesocolic hernia	Mechanical obstruction	Intermittent pain, vomiting	Yes
VI	54	1957	Transmesocolic hernia	Internal hernia	Intermittent upper abdominal pain	No
VII	75	1953	Paracecal hernia	Obstruction of small bowel	Crampy abdominal pain	Yes
VIII	67	1957	Paracecal hernia	Obstruction of small bowel	Crampy abdominal pain, vomiting	Yes

one of their own but did not state the number treated surgically or the mortality. Cutler and Scott [3] collected fifty cases of transmesenteric hernia with an overall mortality of 38 per cent.

Our eight patients were treated surgically without mortality. Only three cases presented as acute intestinal obstruction requiring emergency surgery and four of the remaining five cases were correctly diagnosed preoperatively. It should be mentioned that the standards of preoperative and postoperative care have been raised considerably since many of the cases were reported in the literature.

Apparently all twelve cases reported by Zimmerman and Laufman [9] presented as acute abdominal emergencies and the correct clinical diagnosis was not made in any case. Mayo et al. [8] state that the diagnosis of duodenal hernia is a rare feat and Longacre [6] reports the correct diagnosis in only five of 140 paraduodenal hernias. Our experience, although limited, would indicate that the diagnosis can be made preoperatively when suspected in the non-obstructed cases. It should be emphasized that chronic, intermittent, crampy abdominal

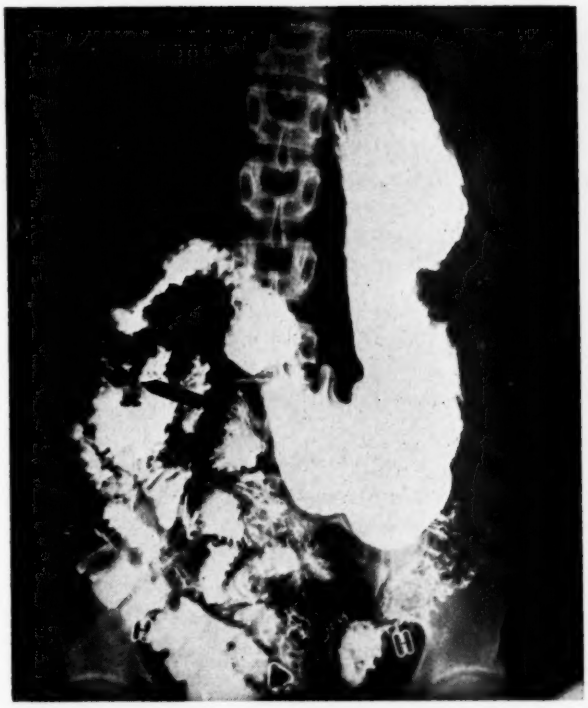

FIG. 2. Case III. Conglomerate loops of jejunum filling the right upper abdomen adjacent to the duodenum indicate a right paraduodenal hernia.

FIG. 3A. Case VI. Transmesocolic hernia studied by barium enema. Note the redundant colon and the conglomeration of small bowel loops in the left upper quadrant.

FIG. 3B. Case VI. Lateral view shows the clump of small bowel extending posterior to the posterior vertebral border.

pain associated with nausea and relieved by vomiting was the presenting complaint in all but one of our cases. The presenting complaint in the remaining case was diarrhea. Barium studies were performed in all five of the unobstructed cases and the diagnosis made in four. Williams [8] has analyzed the findings on x-ray films in internal hernia and has listed in order of importance displacement or disturbance of small bowel arrangement, sacculation or clumping, segmental dilatation, stasis, reversed peristalsis and fixation. He has stressed examination in the lateral erect position. These diagnostic features are shown in Figures 1 through 3.

The surgeon must be aware of the various types and locations of internal hernias and the anatomy of each to facilitate their management when encountered. He must also examine the restraining structures (mesentery, peritoneal reflections) thoroughly with respect to the location of defects producing internal hernia whenever the abdomen is explored for unexplained pain or obstruction remembering that these hernias may reduce spontaneously under anesthesia.

Internal hernias may present as acute intestinal obstruction with progressive symptomatology or as a vague syndrome of intermittent crampy pain, nausea and vomiting, and distention characteristic of incomplete obstruction. Those presenting as acute obstruction are largely of academic interest because the indications for surgery are those of any intestinal obstruction. All of our cases of acquired internal hernia were diagnosed when explored for obstruction.

The congenital group may be extremely difficult to diagnose but the diagnosis of congenital internal hernia should be considered when the patient who has not undergone operation presents with symptoms of intermittent intestinal obstruction—crampy pain, nausea, vomiting, loss of weight. A routine upper gastrointestinal barium study will demonstrate some of these lesions but if negative, a study of the small bowel should be made.

SUMMARY

Eight cases of congenital internal hernia are presented. Three presented as acute intestinal obstruction and five as chronic intermittent abdominal pain with the correct diagnosis established by x-ray examination in four cases. All eight cases were corrected by surgery without any mortality.

Acknowledgment: I am grateful to Dr. William Molnar, Department of Radiology, for assistance in selecting and interpreting the x-ray films.

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Fluid and Electrolyte Balance Following Injuries to the Head

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METABOLIC disturbances of various types have been noted occasionally in patients who have sustained injuries to the head [6]. The exact manner of development of these disorders is obscure. Since the serum concentrations of various electrolytes do not necessarily reflect the total body content of these ions, it was believed that balance studies might serve to elucidate the problem. The principles of the balance study have been thoroughly explained by Moore and Ball [9].

The data presented herein were obtained from a study of three patients who had sustained injuries to the head of varying degrees of severity.

METHOD

Intake was limited to fluids and feeding formula by nasogastric tube, and intravenous fluids. The formulas were analyzed for sodium, potassium, chloride and nitrogen. Indwelling catheters were inserted. The bottles used for collecting urine were kept on ice. Stools were not collected.

Twenty-four–hour urine specimens were analyzed for sodium and potassium by flame photometry, employing the Beckman model DU spectrophotometer with flame attachment [11]. Chlorides were determined by a modification of the Sendroy iodometric procedure [17]. Nitrogen determinations were performed by the Pregl micro-Kjeldahl procedure, using selenium oxychloride as a catalyst. Aliquot samples from the twenty-four–hour urine specimens were measured for 17-ketosteroids [16] and 17-hydroxycorticoids [15]. The procedures for serum electrolytes were the same as listed previously. Carbon dioxide combining power was measured as described by Peters and Van Slyke [14].

The balance data are charted in a manner similar to that used by Moore and Ball. The intake is charted upward from the zero line; the output is charted downward from the intake line. The difference between these values represents the net balance (stool losses were ignored in this study). Positive balance, above the base line, is cross hatched; negative balance, below the base line, is solid black.

CASE REPORTS

CASE 1. A sixteen year old white boy sustained an injury to the head on June 26, 1956, about 8 P.M. Shortly after the accident he was unconscious, and bilateral Babinski signs were elicited.

He was still unconscious when transferred to Letterman Army Hospital several hours later but no other abnormal neurologic findings were noted. He had a linear fracture of the left frontal bone.

The patient's conscious state was impaired for several days and he was confused and disoriented for about one week.

The balance study was begun on June 28, approximately twenty-eight hours following the injury. Data on fluid balance were available from four hours after injury. Collection periods were twenty-four hours in duration. This patient was confined to bed during the entire study.

The results of the balance study are charted in Figure 1. Electrolyte changes were relatively small, possibly falling within the range of error of the methods. The negative nitrogen balance on the first two days of the study appears definite and

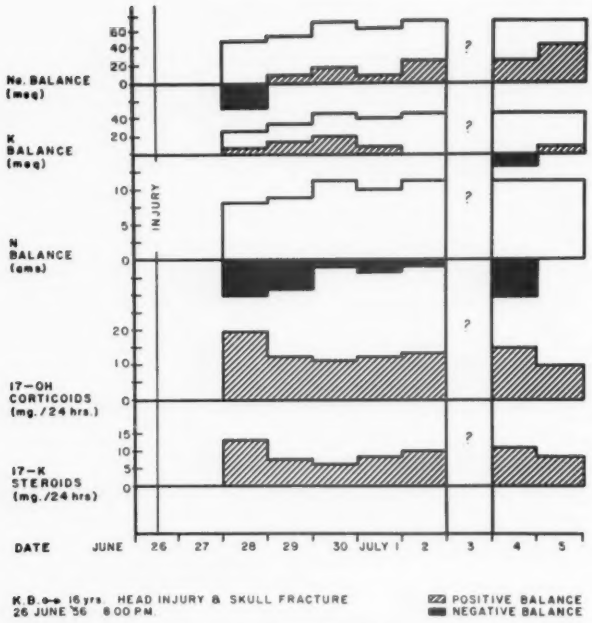
Na. BALANCE (meq)
K BALANCE (meq)
N BALANCE (gms)
17-OH CORTICOIDS (mg./24 hrs.)
17-K STEROIDS (mg./24 hrs.)
INJURY
DATE
JUNE 26 27 28 29 30 JULY 1 2 3 4 5
K.B. 18 yrs. HEAD INJURY & SKULL FRACTURE
26 JUNE '56 8:00 P.M.
POSITIVE BALANCE
NEGATIVE BALANCE

FIG. 1. Data in Case 1. Reading from the top downward: sodium balance, potassium balance, nitrogen balance, 17-hydroxycorticoid excretion, 17-ketosteroid excretion. (See text for explanation of method for charting balance data.) Solid black indicates negative balance, lined area a positive balance. (Specimens were discarded accidently on July 3.)

is the usual response to injury [9]. The 17-hydroxycorticoid excretion was 22.1 mg. on the first day of the study, falling to 12.3 mg. on the following day and remaining in this range during the remainder of the study (normal range in this laboratory, 5 to 14 mg./day in males). The 17-ketosteroid excretion was 13.6 mg. on the first day and 7.1 mg. the following day (normal range, 11 to 27 mg./day).

Serum electrolyte concentrations were checked periodically. On June 27 (the day after the injury) the serum sodium concentration was 148 mEq./L. Potassium was 4.2 mEq./L.; chloride 104 mEq./L. and carbon dioxide combining power 18.9 mEq./L. The tendency toward elevation of the serum sodium concentration was probably due to mild dehydration, since the fluid intake on that day was only 540 cc. and the urine output was 1,450 cc. The depressed CO_2 probably represented respiratory alkalosis (hyperventilation). Two days later all serum electrolyte levels were within normal limits.

CASE II. A twenty-two year old airman was injured in an automobile accident on December 7, 1956, and was transferred to Letterman Army Hospital the following day. He was comatose; a right hemiparesis was noted. The patient improved slowly and was alert, but aphasic, by December 20.

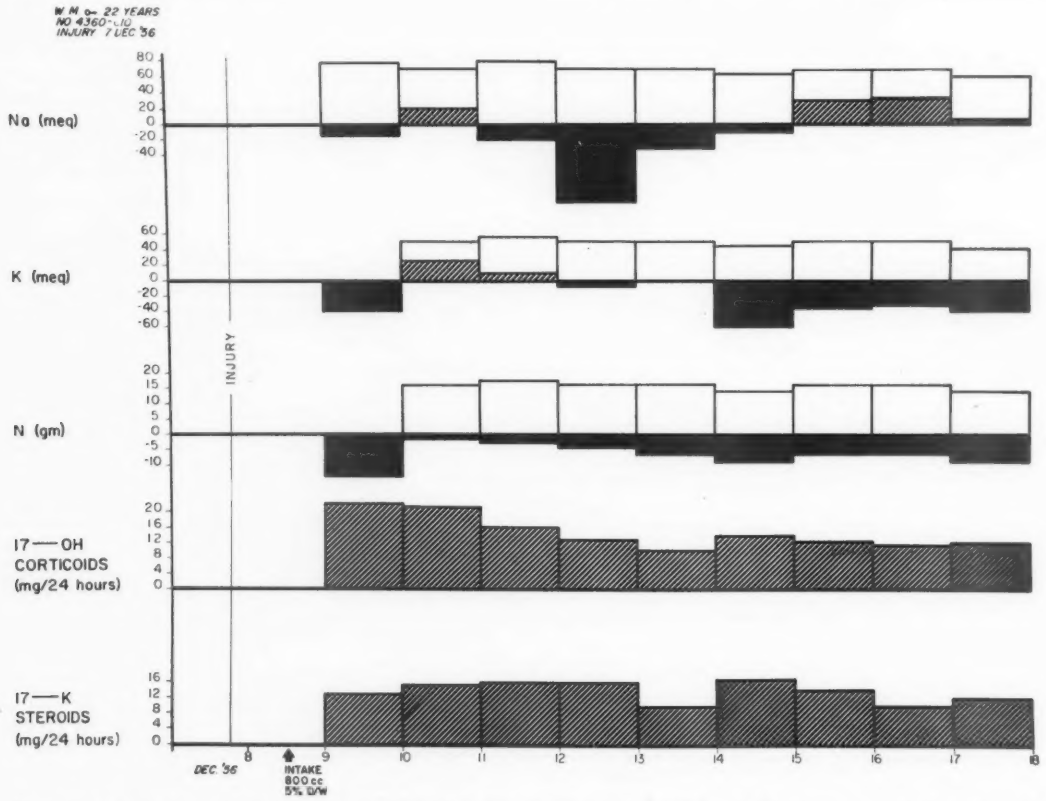

FIG. 2. Data in Case II. Reading from the top downward: sodium balance, potassium balance, nitrogen balance, 17-hydroxycorticoid excretion, 17-ketosteroid excretion. Method of charting as in Figure 1.

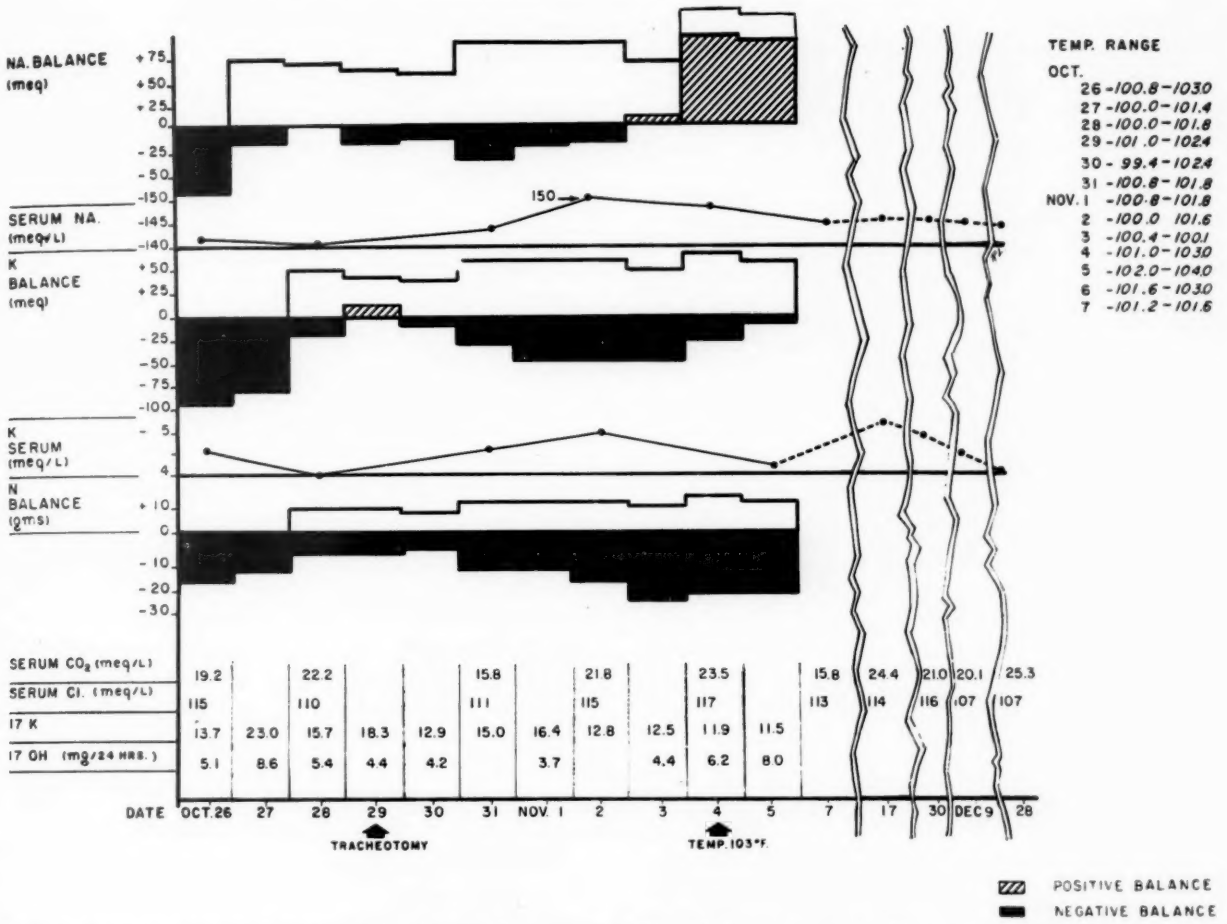

FIG. 3. Data in Case II. Reading from the top downward: sodium balance, serum sodium, potassium balance, serum potassium, nitrogen balance, serum CO_2 combining power, serum chloride, 17-ketosteroid excretion, 17-hydroxycorticoid excretion. The patient's range of body temperature is given in degrees Fahrenheit in the upper right hand corner. Balance data charted as in Figures 1 and 2.

He began to walk with assistance one week later. A right homonymous visual field defect was noted. An electroencephalogram taken January 10, 1957, was interpreted as a low voltage, left frontotemporal focus, and a slow wave focus in the right frontal region. Residual hemiparesis and hemianopsia, as well as mental confusion, were still present by January 31, when the patient was transferred to another hospital.

The balance study was begun on December 9, approximately thirty hours after the injury. The results are charted in Figure 2.

The sodium balance pattern was not striking until the fifth day after injury. At this time a definite sodium diuresis took place, followed by several days of sodium retention. The potassium balance tended to be roughly opposite to sodium balance, but was similar to the nitrogen balance, which was negative throughout the study. The twenty-four-hour 17-hydroxycorticoid excretion was 22.8 mg. on the first day of the study, gradually falling to 10 to 12 mg. within several days. The 17-ketosteroid excretion varied without any consistent pattern.

Serum electrolyte concentrations were not abnormal; however, a comparison of serum sodium concentration with the balance data is interesting. On December 12, during definite sodium diuresis, the serum sodium concentration was 144 mEq./L. On December 14, the serum sodium was 140 mEq./L. On December 17, after two days of moderate sodium retention, serum sodium fell to 136 mEq./L.

CASE III. A thirty-seven year old pilot sustained an injury to the head in an automobile accident on October 22, 1955. He was transferred to Letterman Army Hospital at 3 A.M. the following day. The patient was deeply comatose, responding with only slight movements of the extremities to painful stimulation. His pupils were very constricted and equal. The plantar reflexes were extensor bilaterally. The respiratory rate was 36/min.

Roentgenograms of the chest demonstrated patchy pulmonary infiltration. Roentgenograms of the skull were negative for abnormalities.

Hyperpnea persisted and the patient's body temperature was elevated. (Fig. 3.) Tracheostomy was performed on October 29, following which respiration was less labored. A roentgenogram of the chest demonstrated clearing of the infiltration.

The patient was slightly more responsive by November 3. On the following day his temperature rose to 103°F. and remained elevated for three days. He improved slowly during the months that followed and was ultimately discharged. He was ambulatory but still confused. It was reported to us that he was flying again, one year later.

The balance study was begun twelve hours following injury. (Fig. 3.) The response to trauma was complicated by several factors, including hyperpnea and fever. Sodium balance was moderately negative for eight days and then became strongly positive following a sudden rise in body temperature. The serum sodium concentration, however, rose during the period of negative balance reaching a high of 150 mEq./L. on the eighth day. It then fell during the period of positive balance to 144 mEq./L. on the thirteenth day. The serum chloride concentration was moderately elevated during this time. Potassium and nitrogen balance were negative throughout the period of study.

The serum CO_2 combining power was variably decreased, presumably indicating respiratory alkalosis due to hyperpnea. The 17-hydroxycorticoid excretion was not elevated. The 17-ketosteroid excretion was somewhat high at first, particularly two days after the injury. The serum eosinophil concentration was 61/mm.^{3} twelve hours after injury and reached 477/mm.^{3} five days later.

COMMENTS

There are certain difficulties which are inevitable in performing this type of study in traumatized patients. Obviously, one cannot study their metabolic balance prior to trauma. Since these were presumably healthy young men, a zero balance and normal serum concentrations were assumed to have been present prior to trauma.

Some delay is unavoidable between the time of trauma and the start of the study. In the present series the delay varied from twelve to thirty hours; thus, the metabolic responses immediately following trauma (which may have been the most vigorous ones) were missed. However, certain findings are worth noting.

Sodium Metabolism. Sodium conservation (and positive sodium balance, if sodium is given) occurs almost invariably in non-depleted patients following general surgical trauma, burns or craniotomy [*9,20*]. Sodium retention usually lasts for several days and is followed by a period of negative sodium balance. The serum sodium concentration tends to fall during sodium retention and to rise during the sodium diuresis ("sodium paradox" [*9*]).

Early sodium retention was not found in the present studies. In Case II, the sodium diuresis on the fifth day suggests that sodium conservation may have occurred during the thirty hours between injury and the start of urine collections. In Cases I and III, respiratory alkalosis was probably present, as pointed out previously. It has been demonstrated [*2,8,18*] that increased renal excretion of sodium occurs during respiratory alkalosis; this may explain the negative sodium balance in these cases.

The tendency of the serum sodium concentration to rise during negative sodium balance and fall during sodium retention is illustrated by the data of Cases II and III. Whether this fluctuation is due to shifts of sodium into and out of cells [*9*], the state of hydration [*3,19*], variations in the amount of sodium deposited in bone [*1,13*], or a combination of these mechanisms, cannot be determined from the present studies. The early elevation of serum sodium concentration in Case I was probably due to dehydration, as explained previously. In Case III the elevated body temperature and hyperventilation probably increased insensible fluid loss, so that dehydration may have been partially responsible for the serum sodium concentration of 150 mEq./L., even though the *apparent* fluid exchange (intake vs. urine output) was in balance.

Potassium Metabolism. Potassium balance was initially negative in Cases II and III, then slightly positive, then negative again. In a general way, potassium balance tended to follow nitrogen metabolism. In Case I, that of the patient with the trauma of least severity, potassium balance was mildly positive throughout except for the eighth day. Even in this patient the trend tended to follow nitrogen balance.

Variations of serum potassium concentration were slight and of no apparent significance.

Nitrogen Metabolism. All three patients were in negative nitrogen balance throughout the period of study. This was probably more pronounced than recorded, since stool analyses were not done. During the periods under study the patients were in bed; their conscious states were more or less impaired and spontaneous movements depressed, which may account in part for the negative nitrogen balance [*4,9*].

Water Balance. A state of antidiuresis generally develops following major trauma and usually persists for twenty-four to thirty-six hours [*5,7*]. However, this did not occur in the three cases reported herein. In fact, there was a definite negative water balance during the first twenty-four to forty-eight hours of the balance periods. Since the balance studies were started some hours after the trauma, an early transient antidiuresis may have been missed. However, in Case I the water balance measurements were started four hours after trauma (other studies were started twenty-eight hours after trauma) and a definite negative water balance (intake 540 cc., output 1,450 cc.) was present in the first twenty-four–hour period. Possible explanations of the lack of an antidiuretic phase include trauma to the hypothalamus or pituitary and increased solute load, since sodium retention did not occur. The answer cannot be definitely resolved from the present studies.

Urinary Excretion of Steroids. Increase of the urinary excretion of 17-hydroxycorticoids generally occurs following trauma and correlates fairly well with the degree of trauma [*10*]. This value was elevated early in two of our cases, as expected, but was low in Case III, that of the pilot who had sustained a fairly severe injury to the head. Since the clinical picture suggested a disturbance of brain stem function, it is conceivable that the hypothalamic-pituitary relationship was disturbed.

The 17-ketosteroid excretion was irregular and variable and did not appear to correlate with the other findings or the clinical picture. This corresponds with the experience of others [*10,12*].

SUMMARY

Electrolyte and nitrogen balance, serum electrolyte concentrations and steroid excretion were studied in three patients who had sustained injuries to the head.

The results of these studies differed in certain respects from those in patients who have undergone other types of trauma. In the three patients studied sodium retention or an antidiuretic state did not develop following trauma. In one of the three patients, urinary excretion of 17-hydroxycorticoids was not increased.

Possible explanations for these differences are discussed.

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"Students were taught mainly from the writings of one famous doctor of the past, a Greek named Galen, who had lived under Roman rule, born in 130 A.D. Galen was an opinionated man who wrote voluminously and he had an unshakable conviction of his own worth. 'If anyone desires to become famous,' he wrote, 'all that is necessary is to accept what I have established.' And again, 'Never yet have I gone astray.'

"This consummate egoist, who was in point of fact a very mediocre physician, though a somewhat better surgeon, was accepted at face value in the universities and schools of Europe. His precepts were taught as absolute fact, and he dominated medical thought until well into the Renaissance. This didactic doctor had, however, been progressive enough to cut up a few pigs and apes and to write about the organs he found (without, unfortunately, making it clear that he was talking about animal, not human, anatomy), but for even this bit of original research he should not be given too much credit." (From: Young, A. Scalpel: Men Who Made Surgery, p. 8. New York, 1956. Random House.)

Open Method Treatment of Burns with Aerosol Spray

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A DEFINITIVE, direct, adequate approach to the problem of treatment of thermal burns in our present-day civilization cannot be overemphasized. Much has been written and said on the subject with general over-all agreement. Open and closed methods have their advocates, each with excellent reported results. We propose to report a series of burn cases treated in a general hospital. These patients were all treated by the open method [*3,7,11*] in conjunction with the use of an aerosol spray* containing benzocaine in a special oil base.

The best results are obtained when burn cases are segregated under the care of a team especially trained in this form of trauma. The management of the burn case entails considerable time, effort and expense. The therapy group must have a knowledge of the pathologic physiology of fluid, electrolyte and protein requirements [*4,5,10*]. Skill in the surgical technics of removal of eschar and replacement of skin, and in rehabilitation of the patient is essential [*9*].

Burns are a major problem, especially in the very young and old. Second degree burns which involve over 15 per cent of the body surface and third degree burns involving over 5 per cent of the body surface with mixed injuries such as fractures, respiratory involvement and rectal or urethral involvement, are classed as major burns [2].

* Dermoplast (Mallon Division of Doho Chemical Corporation, New York, N. Y.).

PROCEDURE

On admission the burn patient is treated as an emergency. The resident in charge is alerted, and the staff in attendance is masked. Only sterilized linens are used. The patient is disrobed and put to bed; no morphine is given. The burned areas are immediately sprayed with the aerosol spray. Relief of pain is prompt, and frequently no other sedation is required. Barbiturate sedation is seldom indicated. A complete history is obtained, and a special chart with a diagram of the extent and depth of the burn is made. A venipuncture (cutdown where indicated) is performed. A complete blood count is taken for baseline determinations of blood urea nitrogen, sugar, total protein (A/G ratio), hematocrit, sedimentation rate, rosinophils, sodium, potassium, CO_2 combining power and chlorides. Urinalysis, and typing and crossmatching of blood is also done. At least 1,000 cc. of blood is crossmatched immediately for emergency use. An infusion of Plavolex® is started. Blood studies are performed whenever possible by micromethod in order to preserve the veins for intravenous feeding.

A cradle is placed over the patient, and sterile sheets are placed over the cradle. The burned areas are cultured and sensitivity tests done when pathogens are found. The patient is photographed and weighed on a special scale [*8*]. Tetanus antitoxin or toxoid is given after proper skin testing [*1*]. Blood pressure, pulse and respiration are checked regularly and recorded. A Foley catheter is introduced into the bladder, and hourly fluid intake and urinary output are calculated.

After this initial work-up the patient is assessed clinically. The type and extent of the

burn area are noted and charted. The percentage of burns is calculated via the "Rule of Nine" [12]. The fluid requirements of the patient are then determined by the following method of calculation: the percentage of the body area involved times the number of pounds the patient weighs gives the number of cubic centimeters of fluid the patient needs for the first twenty-four hours. This is an approximation of the total amount, and with subsequent re-evaluation of the patient changes may be made. The total amount of fluids is divided as follows: one-sixth plasma (or blood volume expander), one-sixth whole blood and two-thirds electrolyte solutions.

The nursing care of the affected patient is extremely important. Whenever practicable, a special nurse and one physician are assigned to watch the patient continuously for the first twenty-four to forty-eight hours. In very critical cases the hematocrit, hemoglobin and specific gravity of the urine are noted and recorded every hour. This enables us to determine the patient's condition for maintenance of speed of flow of intravenous fluids and type of fluids to administer. We have seen the picture change very rapidly. This procedure further enables us to check on the assistant resident in charge of the critically ill patient, to make certain he is keeping close observation of his status. The patient is sprayed with the aerosol spray every hour for the first twenty-four hours, then four times daily, and later as indicated by the amount of pain present. Routine care is given to the eyes in burns of the face. Suction of the nasopharynx is used in patients who are comatose in order to keep the respiratory tract as clear as possible. Modification of the patient's fluid intake is determined chiefly by the hematocrit values, urinary output and specific gravity figures obtained by the hourly determinations. We then estimate, as far as can be done clinically, whether certain patients can tolerate the load we are giving the cardiac and pulmonary systems.

In a small percentage of cases the blebs formed on the skin may be débrided under sterile precautions. Good crust formations have been observed to form early. The crusts are soft and pliable, and are well formed even in the creases of the axilla and neck, and over the joints. Débridement is performed between the seventh and eleventh days. Skin grafting is usually performed forty-eight hours after débridement. When the skin grafting procedures are performed, rehabilitation is instituted. The patients are encouraged to use the non-involved joints. Emotional rehabilitation, under proper guidance, is encouraged whenever necessary.

TABLE I

Age Groups	No. of Cases
0–5 yr	16
5–10 yr	3
10–20 yr	2
20–30 yr	2
30–40 yr	5
40–50 yr	0
50–60 yr	1
60–70 yr	0
Over 70 yr	3

STUDY OF CASES

Our series includes thirty-two patients treated within the period from November, 1957 to May, 1958. The ages varied from two and a half months to seventy-five years. (Table 1.) Fifty per cent of the patients were very young, under five years of age.

There were two deaths in the series. The first patient was a seventy year old woman who suffered second and third degree burns of over 90 per cent of her body surface when her clothes ignited in the kitchen of her home. She had recently recovered partially from a cerebrovascular accident. There was a history of a previous nephrectomy. At the time of admission she was suffering from cardiac decompensation. The patient died within forty-eight hours.

The second patient was a twelve year old boy who had 80 per cent of his body surface burned. On admission he required a tracheotomy to help overcome severe respiratory difficulty. The patient died in twelve hours.

The burn cases varied in intensity. No patients were admitted with burns involving less than 5 per cent of the body surface. The usual procedure is to treat persons with minor burns as outpatients, unless there is a complicating injury such as respiratory difficulty or fracture.

The distribution of the percentage of body surface involved is shown in Table II.

TABLE II

Body Surface Involved	No. of Cases
Up to 10%	8
10–20%	15
20–30%	2
30–40%	1
40–50%	4
Over 50%	2 (both died)

TABLE IV

Body Surface Involved	No. of Cases
Up to 10%	10
11–20%	6
21–30%	3
31–40%	1
41–50%	1
Over 50%	1

Narcotics were not given to any of our patients. In several cases small doses of phenobarbital were used for the first seventy-two hours. There was only one case of infection in the entire group, and this was insignificant. It involved the crusts in the axilla of a patient who was very extensively burned.

Blood determinations for the presence of benzocaine were made daily in all cases; all reports were negative. There were no drug reactions in the series.

CONTROL SERIES

As a control series we used the patients admitted from January, 1957 to November, 1957. There were twenty-two cases in this group. The greatest number of patients were under five years of age. (Table III.) The distribution of the percentages of body surface involved is shown in Table IV.

There were five deaths in this series: (1) ninety-two year old patient, 90 per cent of body surface burned, died within twenty-four hours; (2) seventy year old patient, 50 per cent of body surface burned, died on fourteenth day (severe infection); (3) sixty-six year old patient, 25 per cent of body surface burned, died on fourteenth day (gangrene of leg); (4) seventy-two year old patient, 10 per cent of body surface burned, died on second day (coronary disease); (5) eighty-four year old patient, 10 per cent of body surface burned, died on fifth day (cardiac failure).

TABLE III

Ages	No. of Cases
0–5 yr	9
6–10 yr	1
11–20 yr	0
21–30 yr	2
31–40 yr	1
41–50 yr	3
51–60 yr	0
61–70 yr	2
Over 70 yr	4

In this series of twenty-two cases, eleven exhibited various degrees of infection. In one patient infection resulted in gangrene of an extremity. The organisms cultured included Bacillus proteus, B. pyocyaneus, hemolytic streptococcus and staphylococcus.

Narcotics were given to most of the patients, especially those with over 10 per cent of the body surface involved. Several patients required large amounts of morphine, Demerol® or codeine daily, and all patients required sedation with phenobarbital.

Grafts were not applied early except in one case (fifteen days). In several patients it was necessary to wait for five weeks before reconstructive surgery could be instituted.

TREATMENT WITH AEROSOL SPRAY

The treatment of the local phase, i.e., the burn surface, is an extremely important one in management. Numerous medications, both topical and systemic, have been used for control of pain, prevention of loss of fluid and control of infection.

The medication must fulfill certain criteria: (1) must be non-toxic (locally or systemically); (2) must not retard local repair; (3) must not impair surgical débridement or replacement of skin; (4) must aid in control of infection; and (5) must be applied rapidly and without too much difficulty by the nurse or attendant.

The local care of the burned area is instituted without impeding the important systemic therapy in any way. In fact, the aerosol medication used aids in the management of the burned patient. It contains benzocaine 4.5 per cent, with benzethonium chloride 0.1 per cent,

1A

1B

FIGS. 1A and B. Case 1. A, appearance of patient on day of admission. B, one week after admission.

FIG. 1C. Case 1. Appearance of patient three weeks after admission.

2A

2B

FIGS. 2A and B. Case II. A, appearance of patient on admission. B, twenty-four hours after admission.

menthol 0.5 per cent, methylparaben 2 per cent as preservative and 8-hydroxyquinoline 0.83 per cent. This medication quickly eases the pain and enables the patient to be more easily controlled. The only additional sedation required has been small doses of phenobarbital.

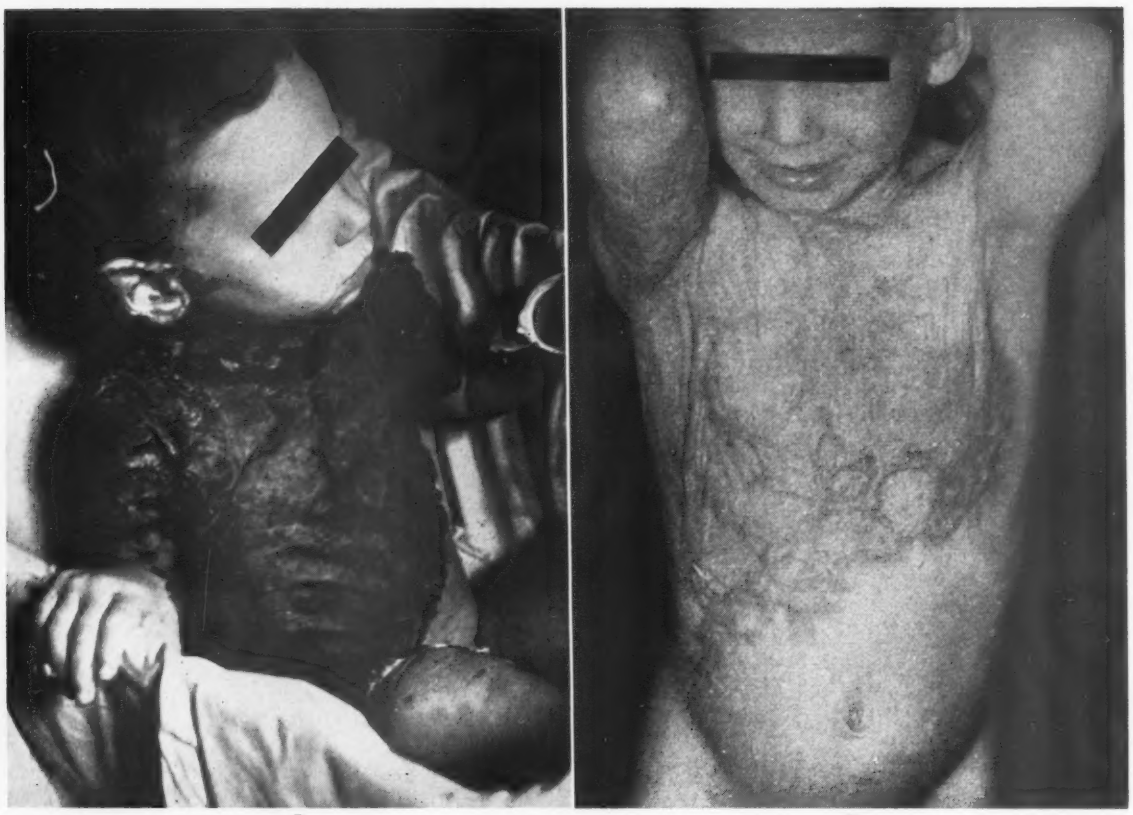
CASE REPORTS

CASE I. I. C., a thirty-eight year old woman, was burned with flaming wax which ignited her clothing. At the time of admission it was estimated that 54 per cent of her body surface was involved in second and third degree burns. (Fig. 1A.) The areas involved included the neck, chest, back, and upper and lower extremities. The patient was treated adequately with fluids and supportive therapy. The aerosol spray was used generously over all involved surfaces and the patient had considerable relief of pain. Only minimal sedation was required; no narcotics were administered.

The crusts formed early, and were soft and pliable. (Fig. 1B.) Culture of the areas involved gave evidence of B. proteus and Aerobacter aerogenes. These organisms were sensitive to Chloromycetin® and were destroyed rapidly. All blood studies for benzocaine were negative.

Débridement was performed on the seventeenth day. Grafting was instituted forty-eight hours later. (Fig. 1C.) The patient made a complete recovery.

CASE II. R. B., a two and one-half year old boy, had 42 per cent of his body surface involved in second and third degree burns. The affected areas included the neck, face, chest, and right upper and lower extremities. (Figs. 2A and B.) The aerosol spray was used generously. No narcotics were



2C 2D

FIGS. 2C and D. Case 11. C, appearance of patient ten days after admission. D, four months after admission.

required; the patient was easily controlled with several small doses of phenobarbital.

Débridement was performed on the sixteenth day, and skin grafting was instituted forty-eight hours later. The patient made a complete recovery. (Figs. 2C and D.)

SUMMARY

The use of the aerosol spray, an adjunct in the open method treatment of burns, is of great value. Pain, the cardinal symptom and *bête noire* of burns, is minimized to an extent that is gratifying to the patient and simplifies the task of the attendants. Daily blood studies for benzocaine are negative, and give assurance that there is no absorption. This is true even in burns involving deeper structures. The eschar forms rapidly and lessens the loss of body fluids, the crust is soft and easy to manage, and infection beneath the crusts is minimal.

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CASE REPORTS

Carcinoma of the Hypopharynx Treated with One-Stage Reconstruction

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THE present methods of treatment of carcinoma of the esophagus are not satisfactory. Surgical management of carcinoma of the lower third of the esophagus gives the best results. In the intrathoracic portion the results are rather poor, and because of the nearness of vital structures the lateral resection of tissues is limited. In cervical carcinoma of the esophagus or hypopharyngeal carcinoma one would expect better results because, if necessary, much of the neck tissue can be sacrificed without interfering with the major bodily functions. Although this region is not easily accessible surgically, nevertheless theoretically the late results should be better than they are. The survival rate of this disease is low and the recurrence rate is high. Radiation therapy and surgery both have their advocates. The objectives of the therapy are to restore the ability to swallow and to palliate or cure those few patients whose localized lesions have limited biological activity [*1*].

The surgical management of carcinoma of the hypopharynx is certainly not standardized. Some surgeons remove the entire esophagus and replace it with the stomach brought up and anastomosed to the hypopharynx [*2,3*]. The two-stage procedure introduced by Wookey [*4*] has its supporters [*5–7*]; however, because of some of its disadvantages, one-stage procedures were designed using different prostheses and grafting procedures. Rob and Bateman [*9*] described the use of a cylinder made of tantalum gauze and surrounded inside and outside with fascia lata. Edgerton [*10*] advocated the use of wire mesh surrounded by split-thickness skin graft. Conley [*11*] uses free skin grafts placed over a woven nylon tube. Ariel [*12*] employs a combined thoracocervical approach and bridges over the defect with a Berman tube surrounded by split-thickness graft. Reidy [*13*] recommends polyethylene tubes or funnels surrounded by skin grafts.

In the following case a modification of the Edgerton procedure was used.

CASE REPORT

T. S. C. (Hosp. No. 023755), a forty year old man, was admitted on August 7, 1957, because of difficulty in swallowing of three months' duration. He was unable to swallow solid food and could drink only clear liquids. He had lost 35 pounds. Blood counts and blood chemistries were within normal limits. No masses were palpable in the neck. On esophagoscopy (by Dr. G. Trainor) an edematous area was found posterior to the larynx, which bled on touch. A biopsy taken from this area showed non-hornifying squamous cell carcinoma. X-ray examination showed a large irregular filling defect on the right side of the hypopharynx, below the valleculae. (Fig. 1.)

Surgery was performed on August 14th. There was a large fungating type carcinoma almost completely obstructing the hypopharynx. (Fig. 2A.) The tumor originated from the posterior wall extending to the right side, ending about 2 cm. from the valleculae and extending down to the level of the cricoid cartilage. There was no visible invasion beyond the muscular wall. No enlarged lymph nodes were seen. Microscopically, the tumor was found to be squamous cell carcinoma

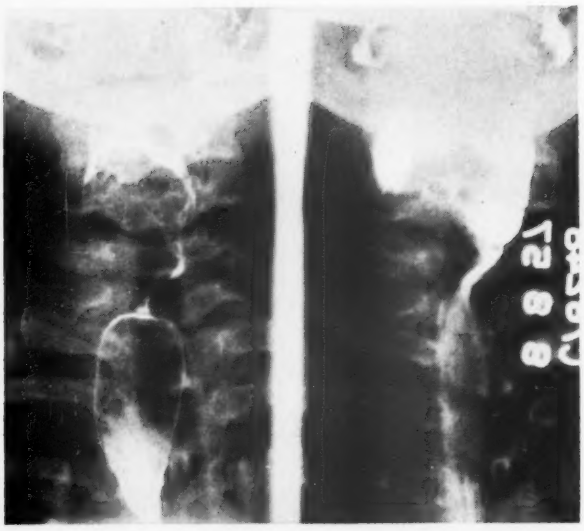

FIG. 1. Barium swallow showing filling defect in hypopharynx.

(Fig. 2B) showing no extension through the muscular layer. The cut edges of the specimen extended well beyond the limits of the tumor.

A large oblong-shaped skin flap of the neck was prepared in such a manner that the base of the flap corresponded to the outer border of the right sternocleidomastoid muscle. The upper border followed a line 2 cm. below and parallel to the ramus mandibulae and extended to the outer border of the left sternocleidomastoid muscle. Here the incision was continued straight down to 1 cm. from the clavicle where it was continued back to the posterior border of the right sternocleidomastoid muscle. The incision included the platysma in the skin flap. In order to prevent drying of the skin flap, it was wrapped in a wet saline sponge. Following this the deep cervical fascia was cut parallel to the anterior border of the right sternocleidomastoid muscle, and the upper belly of the omohyoid muscle was resected with the sternohyoid and sternothyroid muscles. The complete right lobe of the thyroid gland was resected and the inferior laryngeal nerve was exposed in its entire length. The tumor then could be easily felt in the hypopharynx. The dissection was started at the lower portion of the cervical esophagus above the thoracic inlet. After placing a tape around the esophagus, the hypopharynx was dissected off the larynx. The posterior surfaces of the thyroid and cricoid cartilages showed no evidence of tumor tissue and were separated easily from the anterior wall of the hypopharynx. The posterior dissection included the prevertebral fascia which was also removed. After the upper portion of the esophagus and the hypopharynx were completely freed, the esophagus was cut 1 cm. above the suprasternal notch and 1 cm. below the valleculae. Then the defect

FIG. 2A. Gross appearance of hypopharyngeal tumor.

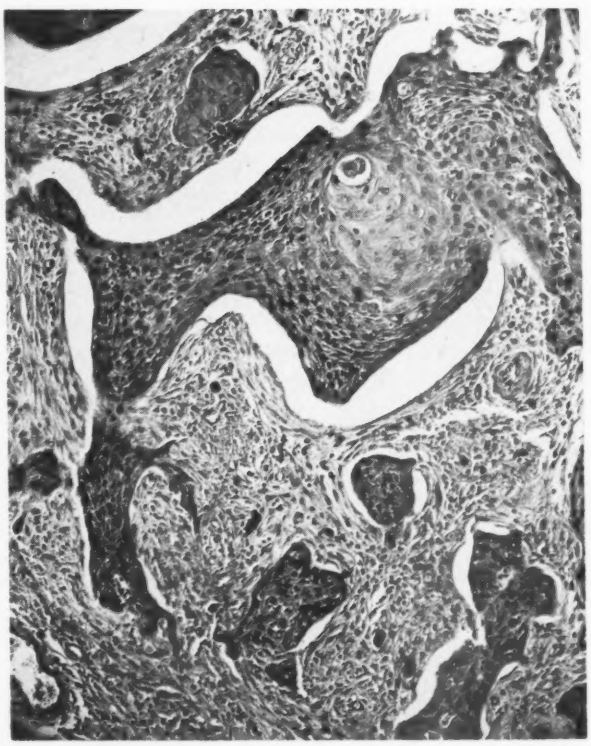

FIG. 2B. Microscopic appearance of tumor showing squamous cell carcinoma.

FIG. 3. Funnel prepared of stainless steel wire mesh.

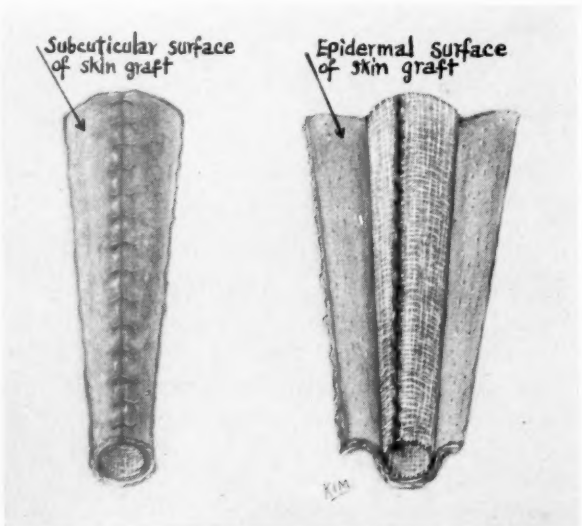

FIG. 4. Wire mesh funnel surrounded by split-thickness skin graft.

in the hypopharynx and the esophagus was replaced by a preformed stainless steel wire (gauge 0.003 inch) mesh funnel (Fig. 3) which was covered with a split-thickness graft $^{15}/_{1000}$ inch thick. The graft was 12 by 17 cm. in size and was placed around the funnel so that the epithelial surface was facing the wire. The graft was fastened to itself by overlapping the edges and sewing them with No. 5-0 silk continuous sutures. (Fig. 4.) The graft also folded over both edges of the wire funnel. The wire mesh was first anastomosed to the lower end of the esophagus by funneling it into the lumen of the lower end. After this the upper end was anastomosed to the remnant of the hypopharynx with No. 4-0 chromic catgut interrupted sutures. (Fig. 5.) A Levin tube, No. 16, was inserted through the graft into the stomach before the anastomosis was completed. The wound was rechecked for hemostasis and the skin flap was sutured with No. 4-0 silk sutures. A tracheostomy was performed below the flap in the suprasternal notch. The patient tolerated this procedure, which lasted three and a half hours, very well.

On the next day the Levin tube was found to be plugged. This was caused by a false knot formation of the tube below the lower anastomosis. After this was straightened out under the fluoroscope, the tip of the tube was found to be below the cardia. Liquid contrast material injected through the tube emptied into the stomach but partially refluxed into the esophagus. For this reason it was decided not to feed the patient through the Levin tube, but to employ a feeding gastrostomy instead. A temporary Stamm type gastrostomy was performed on August 18th. The Levin tube was left in for stenting purposes and was removed on the eighth postoperative day. The patient was ambulatory on the first postoperative day. At first an ordinary gastrostomy feeding formula was used. In a few days, after the patient was used

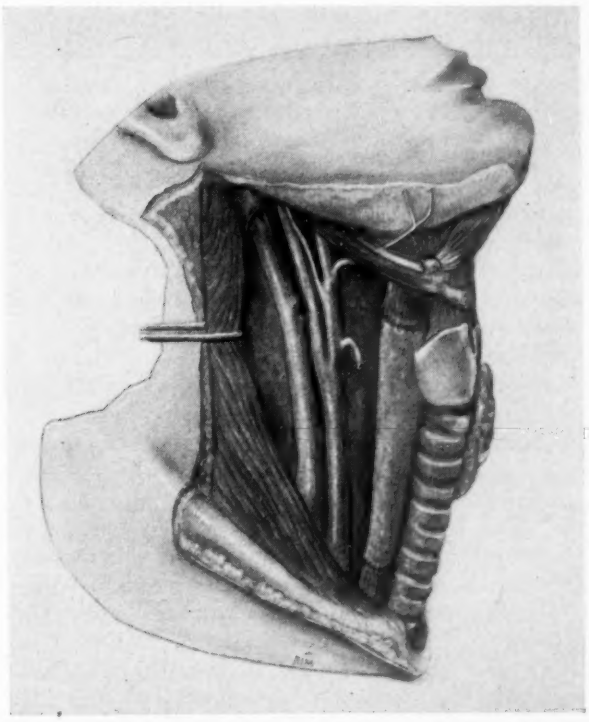

FIG. 5. Drawing showing the wire mesh funnel surrounded by split-thickness skin graft replacing the removed portion of hypopharynx and upper esophagus.

FIG. 6. Dionosol swallow after removal of the wire mesh funnel, showing the good patency of the graft.

to the gastrostomy feedings, his regular meals were emulsified in a Waring blender. He took these feedings quite well and regained strength very rapidly. He was swallowing his saliva without difficulty from the time the Levin tube was removed. The skin flap healed *per primam* and the skin sutures were removed on the seventh postoperative day. At no time was there evidence of infection, edema or inflammation of the neck. The tracheostomy tube was removed on August 26th. On September 11th the wire funnel was removed without difficulty. Through a direct vision laryngoscope one could see that the graft took well and that the epithelial lining was intact with the exception of two pinpoint-sized granulating areas. Oral feedings were started with a full liquid diet at the beginning, and later with a soft diet. The patient had difficulty swallowing at first and he aspirated frequently. He had to relearn the swallowing mechanism, which was obviously greatly disturbed by the removal of the hypopharynx. A Dionosol swallow x-ray examination showed adequate patency of the graft. (Fig. 6.) The

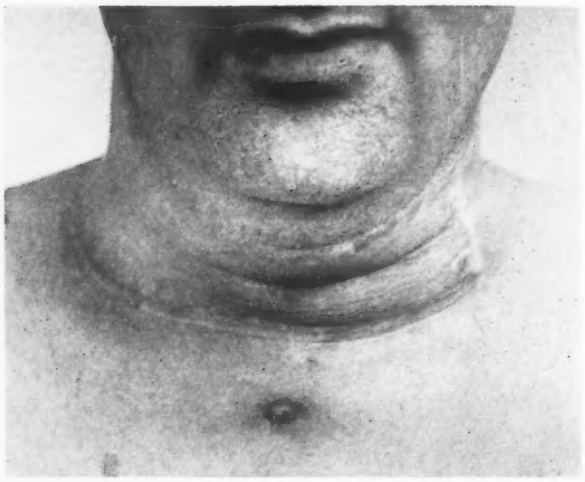

FIG. 7. Neck of the patient after his discharge from the hospital.

patient was discharged to his home on September 21st. (Fig. 7.)

He was seen again on October 11th, at which time he was feeling well and had gained 12 pounds. However, swallowing difficulties developed again in December, 1957, and he was readmitted to the hospital. A hard mass was palpable on the right side of the neck. Laryngoscopic examination showed no evidence of tumor invasion of the larynx. Biopsy of the neck showed a recurrence of the carcinoma. A lymph node removed from the same area showed no evidence of metastasis. A feeding gastrostomy was performed and radiation therapy was instituted. After discharge from the hospital the patient returned to his home town and no further data could be obtained.

COMMENTS

The methods advocating total resection of the esophagus with anastomosis of the stomach to the hypopharynx do not seem logical in the type of lesion described herein. One would gain very little in removing a long segment of normal esophagus below the lesion when only 1 or 2 cm. of uninvolved tissue is usually present above the malignancy. There is a similar problem in the question as to whether the larynx should be removed in all cases of hypopharyngeal carcinoma. If the lesion originates in the posterior wall of the pharynx and if it is an exophytic type of growth, filling the lumen of the hypopharynx and not invading its anterior wall, one would gain very little by performing a laryngectomy. In the case of a tumor originating in the posterior wall one can remove only very little tissue behind the hypopharynx because the vertebral column is only a few millimeters

posteriorly. Although the tumor in this case recurred locally in the tissues of the neck, there was no evidence of laryngeal invasion.

There is no question that the best procedure is to form a tube from the remaining tissues of the hypopharynx. However, this can be done only in cases in which the tumor is very small. The Wookey procedure has many disadvantages. Following the first stage there is great difficulty with the constant drainage of saliva, which will interfere with the wound healing. It is also difficult to keep the tracheostomy clear from the constant salivary flow. Another disadvantage in people with heavy hair growth is the possibility of the hair growth eventually obstructing the lumen of the tube formed from the skin of the neck. So far there is no satisfactory procedure available to prevent this hair growth. The one-stage procedures also have their disadvantages. The type of prosthesis used should not make too much difference as long as it is removable. The best covering material from which to form the lining of the newly formed hypopharynx or esophagus is the split-thickness skin graft. Fascia lata grafts will undergo necrosis too easily. The drawback of the free skin graft is the danger of later stenosis. The newly formed connective tissue has a tendency to scar and to constrict the lumen. This may be prevented by careful dilatation after three to four weeks. It was recommended, with these one-stage procedures, that a nasogastric tube be inserted for feeding purposes and be kept in place for four to six weeks. The dangers of an indwelling nasogastric tube maintained for this length of time, and the discomfort to the patient, are quite obvious. This indwelling tube, however, may also seriously interfere with the taking and the healing of the graft, especially at the site of the lower anastomosis where the lumen is quite narrow. It seems much more logical to keep the nasogastric tube in place for about one week in order to fix the graft. The tube is removed after that time. Feeding can be more easily accomplished through a temporary type feeding gastrostomy. The patient will have no difficulty in swallowing his saliva even while the stent is in place. A temporary tracheostomy, or the permanent type if laryngectomy has been performed, is mandatory.

Several types of skin incisions have been recommended and the surgeon may have his choice. In the case described herein a Wookey type skin flap was used because this type of approach does not commit one to specific type of procedure. If the situation demands it, the Wookey procedure can be performed or one may perform a one-stage procedure. In this case the exposure was excellent and there was no difficulty with the healing of the skin flap.

SUMMARY

A case of hypopharyngeal carcinoma is presented which was treated with one-stage hypopharyngeal resection and replacement with a stainless steel funnel surrounded by split-thickness skin graft. The procedure used followed Edgerton's method with some modifications, which were discussed. The healing and results were excellent until there was local recurrence of the tumor.

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Giant Pharyngoesophageal Diverticulum

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AMONG the causes of dysphagia in the adult male past fifty years of age, the pharyngoesophageal diverticulum is one of those more readily amenable to surgical cure. The literature is replete with discussions concerning pathogenesis, symptomatology, diagnosis, and the merits of one- and two-stage operations. The majority of these diverticula produce sufficient symptoms to necessitate their removal before they have attained a very large size. At the time of operation the sac usually measures between 3 and 6 cm. in its greatest diameter. Quite unusual is the very large diverticulum occupying the superior mediastinum and extending to the aortic arch. We recently treated such a case by one-stage cervical removal.

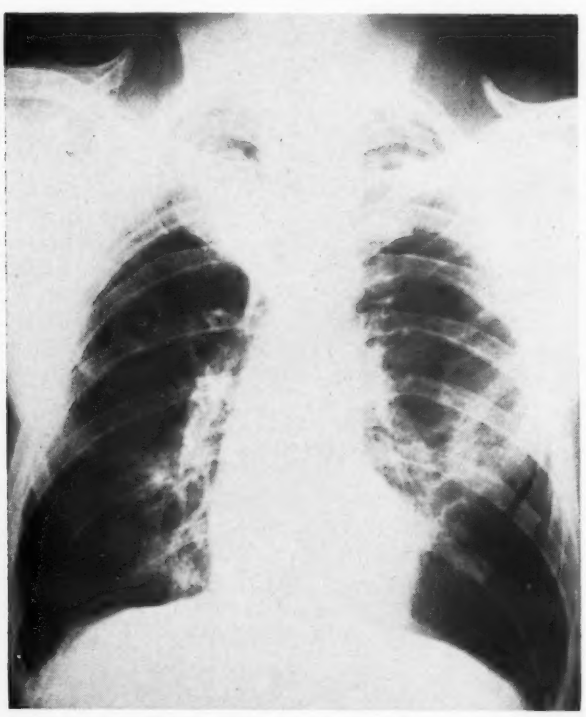

FIG. 1. Plain film of chest showing large sac of diverticulum with air-fluid level seen at medial end of clavicle. Note bilateral pulmonary densities consistent with chronic aspirational pneumonitis.

CASE REPORT

B. P., a fifty-seven year old man, consulted his physician because of severe dysphagia, thirst and weakness of one month's duration. Difficulty in swallowing, first noted fifteen years previously, had been present intermittently, becoming progressively more marked during the past five years and leading to almost complete inability in deglutition in recent weeks.

The patient had lost 30 pounds over the previous six months. He had complained of a chronic productive cough for many years and had been treated for a severe episode of pneumonia in 1949, and for recurrent bouts of pleurisy and pneumonia since that time.

About five years before admission the patient had begun to regurgitate food upon assuming the horizontal position. During this period he had often lost his evening meal upon retiring and had learned that sleeping upright minimized regurgitation and coughing. After swallowing a glassful of fluid he could easily regurgitate it at will by bending forward. He denied any dyspnea or orthopnea and was otherwise well. His exercise tolerance was excellent and he tended to minimize his past symptoms.

Physical examination on admission to the hospital revealed the following: temperature, 37°C.; pulse, 74; respiration, 18; blood pressure, 120/70 mm. Hg; weight, 112 pounds. There was evident weight loss and chronic dehydration. Both supraclavicular fossae were depressed. The chest was almost round with marked increase in anteroposterior diameter and slight interspace retraction. Breathing was largely diaphragmatic. Percussion and auscultation were essentially unremarkable except for a few moist rales audible over both midlung fields posteriorly. The remainder of the examination revealed no abnormalities.

Laboratory examinations showed the following: hemoglobin, 13.2 gm. per cent; white blood cell count, 12,500 per cu. mm. with normal differential

FIG. 2. Overpenetrated posteroanterior film of chest following ingestion of barium which fills the large diverticulum.

FIG. 3. Lateral film of chest showing the filled diverticulum occupying the posterior portion of the superior mediastinum. Note the increased anteroposterior diameter of the thorax and dorsal kyphosis.

count; blood urea nitrogen, 15 mg. per cent; fasting blood sugar, 105 mg. per cent. Urinalysis: Amber; specific gravity, 1.023; pH, 4.5; albumin, trace; sugar and acetone tests, negative; microscopic examination, within normal limits.

Fluoroscopy, while the patient swallowed a cupful of thin barium sulfate, showed all of the latter to enter the diverticulum. None was visualized in the thoracic esophagus or stomach.

Posteroanterior film of the chest (Fig. 1) showed a large sac occupying the superior mediastinum and containing an air-fluid level. Bilateral pulmonary densities consistent with chronic pneumonitis were present. Films (Figs. 2 and 3) following ingestion of contrast material showed the large diverticulum extending to the aortic arch.

After suitable intravenous hydration, operation was performed on September 3, 1957. Preliminary esophagoscopy was performed to rule out distal obstruction. This was negative except for extrinsic pressure due to the sac. Insertion of the esophagoscope into the latter and aspiration of its content allowed excellent visualization of its smooth grey lining. With the patient under general endotracheal cyclopropane anesthesia, a long right cervical incision was made anterior to the sternomastoid muscle and deepened to divide the investing and visceral layers of cervical fascia. The posterior belly of the digastric muscle and inferior thyroid artery were indentified and divided. The strap muscles, thyroid, larynx and trachea were retracted medially and the sternomastoid laterally, exposing the posterior pharynx and the neck of the diverticulum. An esophagoscope was inserted and guided into the main channel past the diverticular opening. Careful dissection was performed in the region of the neck, freeing it from surrounding tissue. A cleavage plane was found exterior to the sac and carried downward by blunt dissection, care being taken to avoid the right pleura, large vessels and regional nerves. Adhesion to surrounding mediastinal structures was quite minimal, and the large globular sac was rather easily delivered into the wound. It was then used to rotate the pharyngoesophageal junction and complete the dissection in this area. The neck was incised at its junction and the sac was amputated. Closure was effected in two layers, using No. 3-0 interrupted silk sutures. A Penrose drain was inserted into the large residual mediastinal space and the wound was closed in layers.

Postoperatively the patient's course was uneventful except for a mild allergic reaction to intravenous fructose on the third day. This subsided with cessation of the infusion and the administration of intravenous Benadryl.® (The patient was allergic to eggs and a son was allergic to aspirin.) He was fed intravenously for the first three post-

operative days, maintained on oral fluids graduated in quality and quantity from the fourth to the seventh day, and then given a soft diet progressing to a regular diet on the tenth day. There was no dysphagia or regurgitation of feedings at any time. The drain was removed on the second postoperative day; the wound healed *per primam* and skin sutures were removed on the seventh day. Achromycin was administered in suitable dosage prophylactically for nine days, and he was discharged on the tenth day after operation (September 13, 1957). Follow-up films of the chest showed the space to fill with fluid which was slowly absorbed with re-expansion of the right pleura.

When next seen by us on September 27, 1957 (twenty-fourth postoperative day), the patient was entirely asymptomatic and stated that he had eaten a full diet of solid food with no difficulty for the first time in several years. This was reflected in his weight gain from 112 pounds to 132 pounds.

The pathologic report was as follows: "Specimen consists of a sac measuring 100 by 40 by 40 mm. having one whitish thickened epithelial concave surface. The opening (neck) measures 15 mm. in diameter. The lining shows extremely thick but regular stratified squamous epithelium with underlying connective tissue which is the site of mild chronic inflammation."

COMMENTS

The long history of dysphagia, its slow progression ending in complete obstruction and the chronic pulmonary changes due to tracheobronchial aspiration, as presented by this case, are characteristic of this disorder. Quite atypical are the very large size of the sac and its wide mouth.

In 1955 Neville [1] reported excision of a pharyngoesophageal diverticulum by right thoracotomy, followed by right and left cervical incisions, in that order. This sac measured 7 by 9 by 10 cm. on x-ray. In 1955 Hawes and Walker [2] reported a diverticulum, measuring 7 by 10 cm. on frontal x-ray, in a patient who presented with severe aspirational pneumonitis and died before surgery could be performed. The sac in our patient measured 10.7 by 10 cm. on the posteroanterior film and 8 cm. on the lateral view. Thus, it appears to number among the largest yet reported.

Regardless of size, these diverticula can almost always be removed by a single cervical approach. Lahey and Warren [3] and Mortensen et al. [4] each reported large series, totaling over 700 cases treated surgically, without mention of a single thoracic incision. We contemplated the use of a combined cervical and thoracic approach in our case, but it was found to be unnecessary. Nevertheless, one cannot deny the possible need for such, if peridiverticulitis and adhesions make dissection from above hazardous. In any event, a cervical approach should always be used first.

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Acute Intestinal Obstruction Secondary to Meckel's Diverticulum with Persistent Obliterated Omphalomesenteric Duct

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IN 1598 Hildanus first described what is now called Meckel's diverticulum. Subsequently, Lavater in 1671, Ruysch in 1707, Littré in 1742 and Morgagni also wrote of it. In 1809 and again in 1812 Meckel set forth the classic description and explained the embryological development of this anomaly.

Approximately 2 per cent of all postmortem examinations reveal Meckel's diverticulum. Its location in the ileum varies but averages about 20 inches proximal to the ileocecal valve. Jay and co-workers [5] have reported one case in which the diverticulum was found 66 inches proximal to the ileocecal valve.

In most cases the diverticulum arises from the antimesenteric border of the ileum. Its size varies from a mere nubbin to 10 or more inches in length. It may be as wide as the ileum itself. It has been found to contain such diverse objects as enteroliths, gallstones, peach pits and even a bullet.

Histologically, the lining tissue of the diverticulum is usually ileum; however, such structures as stomach mucosa, duodenal mucosa, colonic mucosa and pancreatic tissue have been found.

The embryological origin of this diverticulum is from the omphalomesenteric duct. Numerous variations of the anomaly may occur. Eisendrath [3] has recorded four variations, as follows: (1) A complete canal may persist, opening at the umbilicus and communicating with the lumen of the ileum. (2) Either the umbilical or the intestinal portion of the canal may persist, the usual Meckel's diverticulum being formed when the intestinal portion exists alone. (3) An intermediate portion of the canal may persist, giving rise to a retention cyst. (4) The entire canal may be represented by a residual cord, or band, containing the umbilical vessels.

The diverticulum is usually asymptomatic but may produce any of the following complications [4]: (1) acute diverticulitis; (2) acute diverticulitis with perforation and peritonitis; (3) mechanical intestinal obstruction; (4) ulceration and hemorrhage due to heterotopic gastric mucosa; (5) intussusception; (6) congenital fecal fistula.

In infancy and childhood, bleeding is the most common symptom. In adults, intestinal obstruction and diverticulitis are more common.

A persistent omphalomesenteric duct with Meckel's diverticulum is not a common anomaly. Brown and Glover [1] reported an incidence of only .0063 per cent (one case in 16,000) in 31,975 births over a twenty-one-year period. They found two children with complete patency and one child with a persistent but not patent omphalomesenteric duct. During this period thirty instances of Meckel's diverticula were observed, and four patients with persistent omphalomesenteric ducts were operated upon.

Chance and co-workers [2] reported nine cases of acute intestinal obstruction secondary to Meckel's diverticulum at the Mayo Clinic in the period from 1940 to 1952. In four of these nine cases obstruction was the result of the diverticulum or its "terminal ligament" being attached to an adjoining structure. This produced an internal foramen through which a loop of small bowel found its way and became obstructed. Maxeiner, in the discussion at the end of the article by Jay et al. [5], reported a

case of intestinal obstruction due to Meckel's diverticulum in a seventy year old woman. Here the x-ray examination of the abdomen showed shadows in the diverticulum resembling gallstones, but no gas was present in the biliary tract. Facetted enteroliths were found in the diverticulum as the cause of the shadows. Two peach pits were also present.

Lally and Bourke [6] reported a case of acute intestinal obstruction in a sixty-eight year old man. In this case, as in the case we are reporting, the cause of the obstruction was "a heavy fibrous cord extending from the tip of the Meckel's diverticulum to the base of the mesentery."

CASE REPORT

W. M., a sixty-nine year old man, was first seen at 1 A.M. on August 16, 1957, because of crampy abdominal pains which had been present for thirty-six hours.

The patient's past history was of interest in that at the age of five or six years he had been ill in bed for several weeks because of "bowel inflammation." At about the age of twelve he had typhoid fever, and later mumps with orchitis. Also in childhood he had measles and probably pertussis. While in his twenties he had several attacks of pleurisy. At the age of thirty he was very ill with influenza followed by pneumonia. At forty-four years of age he underwent a hemorrhoidectomy. When forty-eight years of age he had a right sacroiliac inflammation which was cured by bedrest. At fifty-two years of age he fractured the right femur in a fall. His convalescence was complicated by thrombophlebitis of the left leg and two pulmonary emboli. When fifty-nine years of age, after an appendectomy, his recovery was again complicated by pulmonary emboli.

The patient had noted for the past six months that his left eye was sensitive to touch. At times, after watching television, he would notice that vision in this eye was cloudy and that the eye would ache. There had been a progressive loss of hearing during the preceding ten years. For the past year nocturia and diminishing power and caliber of the urinary stream had been noted. All other systems were normal except as connected with the present illness.

FIG. 1. Flat film of abdomen showing trace of barium in cecum from recent barium enema and, just inferior to this, the triangular calculus.

For several decades the patient had been troubled with "gas and cramps" in his abdomen and frequent "regurgitation" after meals. These symptoms were not increased or decreased by the appendectomy. Many x-ray studies of the entire gastrointestinal tract had been made. These studies were said to have been negative for abnormalities until three years prior to admission. At this time an x-ray diagnosis of duodenal ulcer was made and confirmed on additional x-ray studies. X-ray films taken a year before admission were said to have shown no trace of the ulcer.

On August 12, 1957, routine gastrointestinal series and gallbladder series had been performed. The patient said he was told he had some "slight eccentricities of the stomach, and gall stones." On August 13th the patient had a difficult bowel movement because of the barium present in the stool. From that time on he passed no flatus and had no bowel movement. Abdominal pains of a colicky nature began slowly on August 14th. On August 15th the patient took an airplane flight, during which the abdominal cramps became much worse. The patient did not vomit.

When first seen at 1 A.M. on August 16th the patient was acutely ill but appeared in good general condition and well hydrated. The temperature was 100°F. and pulse 96. The positive findings were as follows: The abdomen was moderately distended. Gurgles could be heard synchronously with the patient's abdominal pains. No abnormal masses were palpable. There was no spasm, rigidity or rebound tenderness. On rectal examination the rectum contained no stool. The prostate was diffusely enlarged.

The patient was admitted to University Hospital with a tentative diagnosis of acute intestinal obstruction, either low in the small bowel or in the large bowel. An upright film of the abdomen was taken immediately and showed distended small bowel loops with fluid levels. A radiopaque mass, somewhat triangular in shape and about 1.5 cm. on each side, was noted in the right lower quadrant of the abdomen. (Fig. 1.) The possibility of its being a gallstone was considered but no gas was seen in the biliary tract. Only the slightest trace of the recent barium enema was seen in stippling in the cecum. These findings indicated a low small bowel mechanical obstruction, possibly due to an adhesion from the previous appendectomy. A

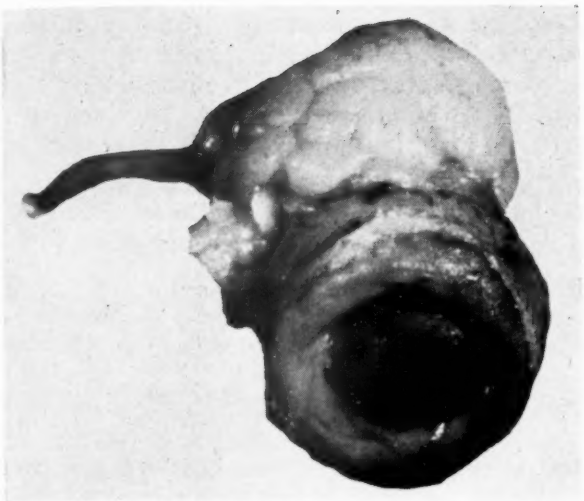

FIG. 2A. Resected Meckel's diverticulum. Note thick band extending from fundus (obliterated persistent omphalomesenteric duct).

FIG. 2B. Calculus found in diverticulum.

long intestinal tube was passed. Intravenous fluids were started. On admission the laboratory findings were: red blood count, 4.9 million per cu. mm.; hemoglobin, 15.7 gm. per cent; white blood count, 13,500 per cu. mm., with 87 per cent polymorphonuclear leukocytes and 13 per cent lymphocytes; sodium, 126 mEq.; chlorides, 102 mEq.; CO_2 combining power, 19.4 mEq.; blood urea nitrogen 18.5 mg. per cent.

Six hours later the patient's general condition appeared improved; he was comfortable and well hydrated. However, the long intestinal tube had not passed the pylorus. There was slightly more distention of the small bowel. Because of continued intestinal obstruction, immediate surgery was decided upon. Just prior to operation ace bandages were applied to both legs because of the history of previous pulmonary emboli.

At operation numerous dilated loops of proximal small bowel were present. On exploration a large Meckel's diverticulum was found; the diverticulum was 2.5 cm. broad at its base and 5 cm. long. It had arisen on the antimesenteric border of the ileum about 50 cm. from the ileocecal valve. Extending from the fundus of this diverticulum was a band 0.5 cm. in diameter containing several blood vessels. (Fig. 2A.) It was thick and fibrous, and ran to the base of the adjoining mesentery of the small bowel. This band was the cause of the mechanical intestinal obstruction; it had become wrapped around a loop of distal ileum, causing complete obstruction. No portion of the bowel was gangrenous. The band appeared to represent an obliterated but persistent omphalomesenteric duct. The band was divided and Meckel's diverticulum was resected in the long axis of the bowel. The defect was then closed in two layers in a transverse direction. Following the closure of the defect in the ileum, the remainder of the abdominal contents were examined and found to be normal. The incision was then closed without drains. The patient's condition was good at the end of the operation.

Postoperatively the patient was treated with anticoagulants because of the history of several episodes of pulmonary emboli. The ace bandages were maintained on both legs for approximately ten days. The postoperative course was complicated by a transient episode of acute glaucoma of the left eye and urinary retention due to an enlarged prostate. The patient was discharged from the hospital on the eleventh day. Just before discharge a flat x-ray film of the abdomen was taken which showed that the calculus noted on the preoperative films was no longer present.

The pathologist, on opening the diverticulum, found a calculus 1.0 cm. in diameter. (Fig. 2B.) There was marked edema of the diverticulum. The lining mucosa was typical of ileum. The fibrous cord at the fundus was reported to be compatible with a persistent obliterated omphalomesenteric duct.

The patient was last contacted on January 2, 1958, at which time he reported that the previous gastrointestinal distress was no longer present.

COMMENTS

This case presents several interesting aspects. First, the patient was sixty-nine years of age before there was complete obstruction from a congenital defect. Also, an appendectomy had been performed eleven years earlier and the diverticulum had not been seen at that time. In addition, a band was present at the tip of the diverticulum, apparently representing a persistent obliterated omphalomesenteric duct. A calculus was present in the diverticulum and

could be seen on the preoperative films. It is of interest that an airplane flight with resultant distention of the gas-filled bowel probably completed the mechanical obstruction. It certainly aggravated it.

This case demonstrates once again that in cases of mechanical obstruction the passage of a long intestinal tube should not delay surgery beyond the time needed to hydrate the patient and prepare him for operation.

CONCLUSIONS

1. A case is presented of a sixty-nine year old man with acute mechanical obstruction of the small bowel due to Meckel's diverticulum with a persistent obliterated omphalomesenteric duct.

2. Neither a patient's age nor even a history of a previous abdominal operation should completely allay the suspicion of the existence of this anomaly.

3. Use of a long intestinal tube is no substitute for prompt surgery in cases of acute mechanical obstruction of the intestine.

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Omphalocele with Duodenal Stenosis

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FOUR patients with omphalocele have been seen in Memorial Hospital in the past year. Our most recent and interesting case was that of a newborn infant with a large omphalocele complicated by evisceration of the small and large bowel, gallbladder and a portion of the liver. Additional anomalies of duodenal stenosis, malrotation of the cecum and Meckel's diverticulum were also present. This patient required two operative procedures to correct the anomalies and made an uneventful recovery.

Omphalocele is reported as occurring about once in every 10,000 deliveries [*1*]. The definition of omphalocele is uniformly accepted to be an eventration of part or all of the abdominal contents at the base of the umbilical cord. It is covered by a transluscent membrane consisting of peritoneum internally and amniotic membrane externally [*2*]. Embryologically, the problem of omphalocele has not been fully clarified. Some believe that it is due to failure in the closure of the anterior abdominal wall, especially the supraumbilical portion [*2,6*]. There are others who believe that the condition occurs between the sixth and tenth weeks of gestation when the abdominal viscera grow more rapidly than the peritoneal cavity, resulting in a protrusion of the intestines into the umbilical cord. If for any reason this disproportion persists, the infant will have an omphalocele at birth [*3,6,7*].

Associated anomalies of other parts of the body occur frequently, some series reporting an incidence of up to 50 per cent [*4*]. Several types of anomalies have been reported [*4–6*] but no mention has been made of duodenal stenosis.

The sac of an omphalocele can contain liver, intestine or other abdominal viscera. This sac, which measures from a few centimeters to as much as 15 cm. in diameter, usually has a wide communication with the abdominal cavity. Small omphaloceles with fewer contents have a much better prognosis [*4,5,7,8*].

Operation is mandatory; otherwise, death ensues [*4*]. Within a few hours the sac will rapidly dry out and rupture with inevitable peritonitis. The bowel also becomes edematous and distended with gas within a few hours and replacement becomes very difficult. The objective of the operation is to replace the viscera into the peritoneal cavity and to make a perfect closure of the abdominal wall defect. If a large defect associated with evisceration is present, replacement of the viscera can increase intra-abdominal pressure to a dangerous degree, resulting in one of three complications: (1) intestinal obstruction, (2) elevation of the diaphragm with diminution of the vital capacity or (3) compression of the vena cava with failure of venous return to the right side of the heart causing death from circulatory collapse. In such a situation a two-stage procedure is recommended by Gross [*10*] and was performed in the case presented herein. Peters describes a technic using cutis grafts for secondary repair of large defects [*9*].

Duodenal stenosis, an associated anomaly in our patient, is another rare condition. The exact incidence is not known because it is often confused with atresia, which is a totally different condition. Stenosis is a narrowing of the lumen, in contradistinction to atresia which is a complete obstruction of the duodenum.

The diagnosis of duodenal stenosis is based on the history and roentgenological findings. Symptoms can occur any time after birth to adulthood and consist mainly of vomiting or regurgitating. However, most of the reported cases occurred in infants during the first or

second week of life [*11,16–18*]. Farber's test, if performed correctly, is helpful in differentiating between stenosis and atresia [*13*]. The x-ray findings are characteristic in that there is usually a dilatation of the stomach and part of the duodenum; this is described as the double bubble appearance [*14–16*].

The accepted form of treatment is surgical and usually consists of duodenojejunostomy, duodenoduodenostomy or, less preferably, gastrojejunostomy [*10,12,18*].

CASE REPORT

A full term white female infant was referred to the hospital approximately thirty minutes after delivery. Practically all of the abdominal viscera were outside the abdominal cavity with no apparent membrane covering them. Part of the intestine appeared ischemic at birth. The infant was taken to surgery within two hours after birth. The protruding organs consisted of all the small intestine, colon, gallbladder, part of the stomach and part of the liver. The entire intestine was edematous and distended. About 10 inches of the terminal ileum were quite dark in color and the question of viability was difficult to evaluate. (Fig. 1.) It was noted that there was a malrotation of the cecum and a Meckel's diverticulum. Because of the critical condition of the infant, we believed that resection of the ischemic segment was not feasible. The organs were replaced into the abdominal cavity with considerable difficulty. It was impossible to close the fascia over the defect because of the marked intestinal distention. The skin alone was used to cover the viscera. The stomach was aspirated at frequent intervals through an indwelling nasogastric tube for the first three days and feedings were started on the fifth day. On the tenth day the patient began to vomit bile-stained material at frequent intervals. X-rays revealed gastric and duodenal dilatation and a swallow of lipiodol revealed obstruction of the third portion of the duodenum. (Fig. 2.)

FIG. 1. Ischemic terminal ileum two hours after birth and just prior to surgery.

FIG. 2. Lipiodol study showing a duodenal stenosis in the third portion of the duodenum. Note the air filling the stomach and the first portion of the duodenum.

Laparotomy was performed through an upper transverse incision. There was marked dilatation of the stomach and proximal portion of the duodenum, with a stenosis at the third portion which barely admitted the tip of a hemostat. Side-to-side duodenoduodenostomy was performed, thus bypassing the stenotic area. The previously described abdominal defect was closed in layers as it was necessary to extend the incision downward to obtain adequate exposure. The postoperative course was uneventful and the baby was started on a formula the third day. She gained weight steadily and was discharged nineteen days following the second operation weighing 5 pounds, 8 ounces. When seen again at the age of four and a half months she weighed 16 pounds and was apparently in good health with a strong abdominal wall.

SUMMARY

A case of omphalocele with associated duodenal stenosis, thought to be the first of its kind, is reported. Two operative procedures were required to correct the anomalies. Early surgery is mandatory in the treatment of large omphaloceles and preferably should be performed within the first hour following delivery.

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Malignant Melanoma of the Breast

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MALIGNANT melanomas arising in the skin, buccal mucous membranes and retina are frequently encountered. In recent years scattered reports of cases of malignant melanoma of the esophagus have appeared. This site is the fourth most frequently involved. Primary involvement of other organs is extremely rare. Recently a patient entered Vanderbilt University Hospital for treatment of a primary melanoma which arose from the glandular tissue of the left breast. A review of the medical literature has revealed a few scattered case reports of malignant melanoma primary in the skin of the breast, but there is only one previously documented case in which primary involvement was in mammary tissue [3]. The rarity of this condition and the application of the various theories of melanoma formation to this particular organ makes this case of special importance.

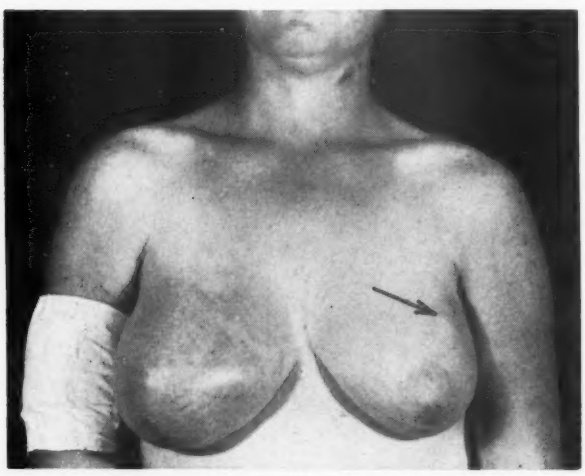

FIG. 1A. Photograph of patient taken on admission to hospital. The arrow denotes the primary lesion in the upper outer quadrant of the left breast. The metastatic involvement of the right breast and neck are also visible.

CASE REPORT

J. O. (Vanderbilt Univ. Hosp. No. 234753), a twenty-six year old single white woman, was admitted to the hospital from the Tumor Clinic with a complaint of "breast tumors." Two years previously she had noted a slowly enlarging mass in the left breast but did not consult a physician until three months prior to admission to the Vanderbilt Hospital. At that time masses had also developed in the right breast, neck, submandibular area and right arm. At another hospital one of the cervical lesions had been biopsied, and a pathological report of undifferentiated carcinoma was made; no treatment was given and the patient was discharged. Because of progressive enlargement of the now bilateral breast tumors and increasing pain related to them, she presented herself at the Vanderbilt University Hospital. A 1 by 1 cm. subcutaneous lesion on the right arm was excised for diagnosis in the Outpatient Department. This proved to be metastatic amelanotic melanoma. The patient presented no other complaints. There was no weight loss or anorexia.

Physical examination on admission to the hospital revealed a healthy appearing young white woman in no distress. A 1 by 2 cm., purplish, non-tender area was noted on the left side of the

FIG. 1B. Incised specimen of left breast from the pectoral aspect showing pigment in the primary lesion.

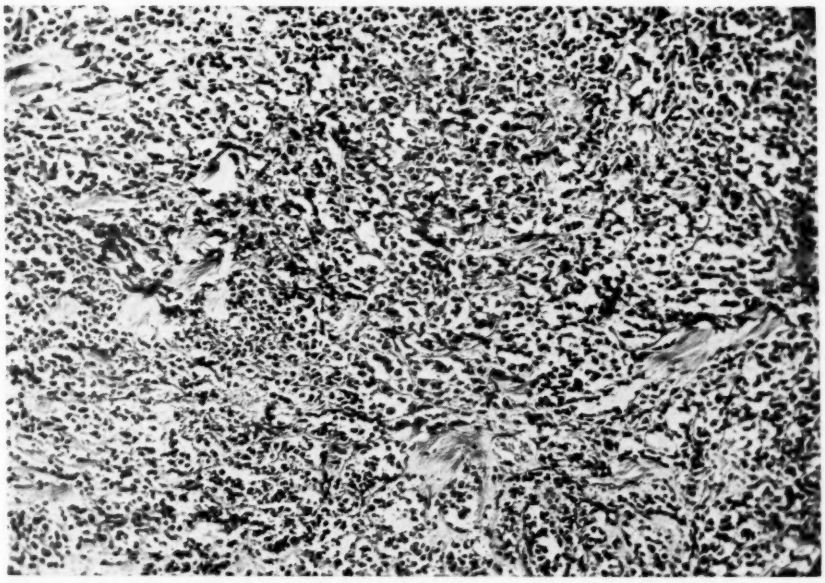

FIG. 2. Photomicrograph of left breast lesion showing bizarre infiltration with melanoblasts and melanin.

neck at the site of previous biopsy. There were two 1 by 1 cm. subcutaneous nodules in the suprasternal area, bilateral soft axillary nodes and a recent surgical incision on the right upper arm. Examination of the breasts revealed the right breast to be approximately three times normal size, hard, tender, red and with typical "peau d'orange" skin changes. The left breast contained the original tumor of two years' duration. There was now a 4 by 4 by 6 cm. hard, irregular mass in the upper outer quadrant of the left breast, with some deep fixation but no skin changes. (Figs. 1A and 1B.) Pelvic examination revealed fullness in the left adenexal area. Because of the nature of the findings on the biopsy performed in the Outpatient Department, careful examination of the skin and mucous membranes was made by eight examiners. No areas suggestive of a primary malignant melanoma or even a suspicious nevus could be identified. The remainder of the physical examination was within normal limits. Roentgenogram of the chest failed to reveal any metastatic nodules.

The patient was in excellent general condition. In an attempt to relieve the discomfort of the large breast tumors and to prevent ulceration of these lesions, bilateral simple mastectomy and bilateral salpingo-oophorectomy were performed. Examination of the abdomen at the time of surgery revealed multiple black peritoneal implants and masses in both ovaries. Microscopic examination of the excised specimens revealed malignant melanoma of the breast with metastases to the contralateral breast and both ovaries. (Fig. 2.)

The patient did well after operation and was discharged on the sixth postoperative day. She continued to do well for a month when she was readmitted for local excision of a painful nodule in the neck. In the subsequent two months diffuse non-pigmented metastases developed in the right axilla, left mastectomy scar, right upper arm, neck, both lumbar areas and left lower quadrant of the abdominal wall. She later returned with progressive abdominal distention, and 4,600 cc. of serosanguineous fluid was removed by paracentesis. The patient made frequent visits to the Outpatient Department for removal of peritoneal fluid. Five months after mastectomy she was rushed to the Emergency Room, but was pronounced dead on arrival. Postmortem examination revealed massive involvement with metastatic melanoma of the myocardium, lymph nodes, lungs, small and large intestines, omentum, liver, adrenals, pancreas, uterus, skin, vertebra, ribs, diaphragm, pleura and thoracic wall.

COMMENTS

In reporting a malignant melanoma arising in an unusual site the first question which might be raised is, "Has the primary site been overlooked?" This is theoretically possible in the patient reported herein, but it seems most unlikely in view of the prolonged questioning and the repeated examinations made by a series of examiners in search of a primary lesion other than in the breast. It seems that if there can be some reasonable explanation for the origin of a melanotic tumor in the breast, such a site must be accepted as the primary focus in this patient.

FIG. 3. The invagination of epithelium which forms the embryonic breast is shown. It is the inturning of these cells which may carry inward the melanin-producing cells. These melanoblasts which arise posteriorly in the neural crests migrate to the anterior chest wall. Figures refer to millimeter size of the embryo at this particular stage. (From: FRAZER, J. E. A Manual of Embryology, 3rd ed. London, 1953. Baillière, Tindall & Cox, Ltd.

There are, at present, two theories concerning the origin of malignant melanoma. Allen and Spitz [2] have been the leading exponents of the epidermal theory of origin while Masson has expounded on and offered evidence supporting the origin of cells in the neural crests. The inception of a melanoma in the glandular portion of the breast may be explained on the basis of either of these two currently acceptable theories. The chromataphoric and endothelial theories of origin have been virtually discarded.

In the embryo, breast development starts in about the second month of growth. It begins in the ventrolateral portion of the body wall in the "milk lines" as an epithelial change. (Fig. 3.) There is first a thickening of the epithelium, and by the fourth month there are evident buds of epithelium which will form the main ducts. From these the entire glandular portion of the breast will eventually develop. (Fig. 4.) It is evident that the pigment-producing cells from the neural crests or epidermal layer may be carried in with this epithelium and lie latent there until they assume the growth characteristics of a melanoma. There is, then, adequate embryologic evidence to support the occurrence of a malignant melanoma primary in the breast tissue itself.

There have been reported rare instances of melanoma metastatic to the breast [7]. The history of the patient reported herein is such as to make it improbable that the primary evidence of neoplasm was a metastatic tumor of the breast which occurred two and a half years prior to a extremely rapid, fatal terminal illness.

In a review of the literature Geschickter [5] refers to a melanosarcoma of the breast but gives no additional details or photomicrographs. The only previously documented case of a primary malignant melanoma of the breast was reported by Gatch [3]. The patient reported by him survived thirteen years after simple excision of the tumor. She died of carcinomatosis, apparently from a second cancer arising in the colon. At autopsy no evidence of melanoma could be found [4]. Our patient exhibited rapid deterioration to a

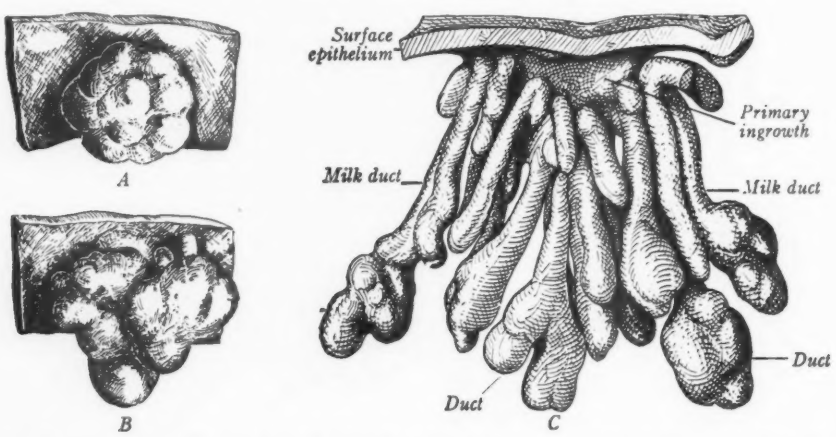

FIG. 4. The primary ingrowth of cells which started as a bud develops into the duct system of the breast. The melanin-producing cells may lie in any portion of the duct system after being carried in during breast development. (From: AREY, L. B. Developmental Anatomy, 5th ed. Philadelphia, 1946. W. B. Saunders.)

fatal terminus, and it is doubtful that the surgical intervention undertaken in this particular person was at all helpful.

SUMMARY

1. A case of malignant melanoma arising in breast tissue has been presented. It is apparently the second such documented case.

2. The existing theories of melanoma formation are not at variance with development in this rarely involved organ.

3. The treatment of choice, as in melanoma of other sites, should be wide excision.

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"Clowes had fairly good results . . . in the treatment of fractures. In cases of fracture of the thigh he would have two towels tied above and below the fracture so that his assistants by pulling upward and downwards separated the fractured ends of the bone. He himself then manipulated the bones into correct position, and applied splints of willow and bandages soaked in egg-white and vinegar. Finally, the injured leg was laid in a bed of rushes. If, as sometimes happened in adults, the union was such that the affected leg was shorter than the uninjured one, then Clowes explained to the grumbling relatives that the results in adults were never quite as good as in children. In the treatment of syphilis, on one occasion at least, Clowes was not successful, for it is recorded in the annals of the Barber-Surgeons that one William Goodnep complained before the Masters of the Company that Clowes had failed to cure his wife of this condition. The Company was no respecter of persons, and Clowes, sergeant-surgeon to the Queen though he was at the time, was ordered to either cure the woman or pay a fine of twenty shillings. Wisely, Clowes paid the fine." (From: Graham, H. Surgeons All, p. 155. New York, 1957. Philosophical Library, Inc.)

Metastasis to a Phalanx Simulating Infection in a Finger

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THE incidence of metastases to the fingers is quite rare [*1*]. There are at the present time thirty reported cases of metastases to the fingers, the predominance being from bronchogenic carcinoma [*2–4*]. We would like to add an additional case to the literature, as this condition is often misdiagnosed as a finger infection such as a felon or osteomyelitis. Bronchogenic carcinoma is noted for its tendency to metastasize to many different sites, but its spread to the fingers is extremely unusual.

FIG. 1. X-ray film of the left hand showing the extensive destruction of the distal phalanx of the middle finger.

CASE REPORT

M. G., a forty-nine year old Negro man, had onset of pneumonia in September, 1957, which did not respond to antibiotics. A right clavicular node was removed in November, 1957, and microscopic examination revealed an undifferentiated carcinoma which was consistent with a metastatic lesion from the respiratory tract. A few days later bronchoscopy was performed and similar tissue was removed from the right

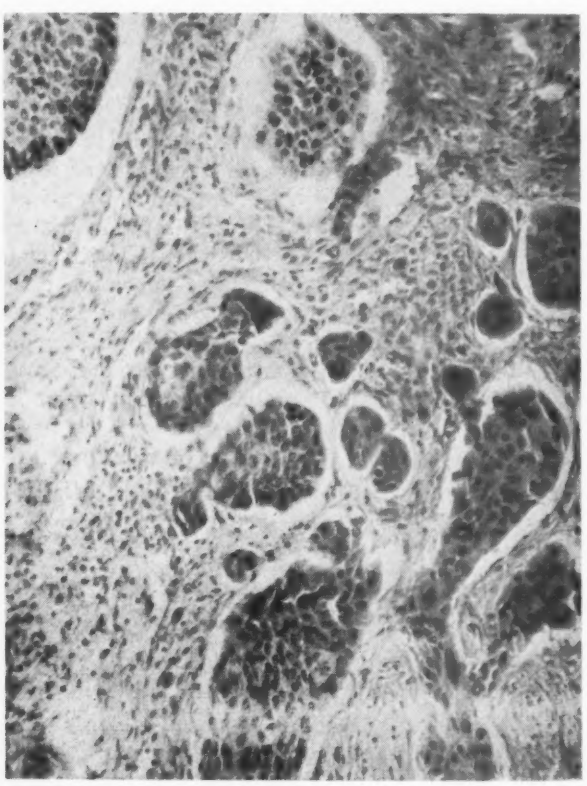

FIG. 2. Photomicrograph of a portion of the distal phalanx of the left middle finger.

middle bronchus. A course of radiation therapy was then started.

In February, 1958, the patient received a minor injury to his left hand and subsequently an infection developed under the nail of the left middle finger. He was seen in the emergency room, where the lesion was surgically drained and he was treated with antibiotics. The true diagnosis was not realized until an x-ray film (Fig. 1) was taken three weeks later, when the lesion still had not improved despite therapy. The distal phalanx was removed by an amputation through the middle phalanx. Sections of this specimen revealed an epidermoid lesion with a large number of mitotic figures. (Fig. 2.) A skeletal survey revealed metastases to the skull, right greater trochanter and the right radial head.

Radiation therapy was continued but the patient had a progressively downhill course and died at home on April 29, 1958. A postmortem examination was not made.

COMMENTS

The incidence of metastases to the hand is quite rare and therefore the diagnosis is not usually made early. However, the possibility must be considered in evaluating finger infections especially where there is known pulmonary disease.

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A Repair for Loss of the Tactile Pad of the Thumb

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Loss of the distal tactile pad of the thumb is not an uncommon injury and may be a disabling one. The injury consists of loss of all or of a significant portion of the soft tissue from the palmar aspect of the distal phalanx of the thumb. This injury is serious in any finger. The thumb is singled out because of its acknowledged importance to the function of the hand, and because of certain inadequacies in usual reparative technics.

The palmar skin is a specialized structure nowhere else available and nowhere more important than on the distal phalanges. After loss of this tissue from the thumb, ordinary repairs are in many ways deficient. The split-thickness grafts are usually fragile and often tender. The usual pedicled full-thickness grafts are also rather fragile, often bulky, unsightly and tender, and frequently involve immobilization in an awkward position. Both technics also are often inadequate in terms of neurotization and final useful sensation. Sensation, when it returns, is of different quality from that lost. The cross finger or palmar flap grafts yielding, as they do, skin more similar to that lost, effect better results in terms of durability and sensation. Most important, however, none of the grafts mentioned are suitable when there is severe loss of pulp as well as skin exposing periosteum.

In evaluating a repair, certain elements must be considered. First, the repair tissue should best be similar to the specialized structure lost. Second, the utilization of this tissue for repair must not impose a disproportionate handicap. Third, satisfactory neurotization with return of function should be possible. Fourth, the repair should not carry undue risk or too prolonged disability. Fifth, cosmetic results should, if possible, be acceptable.

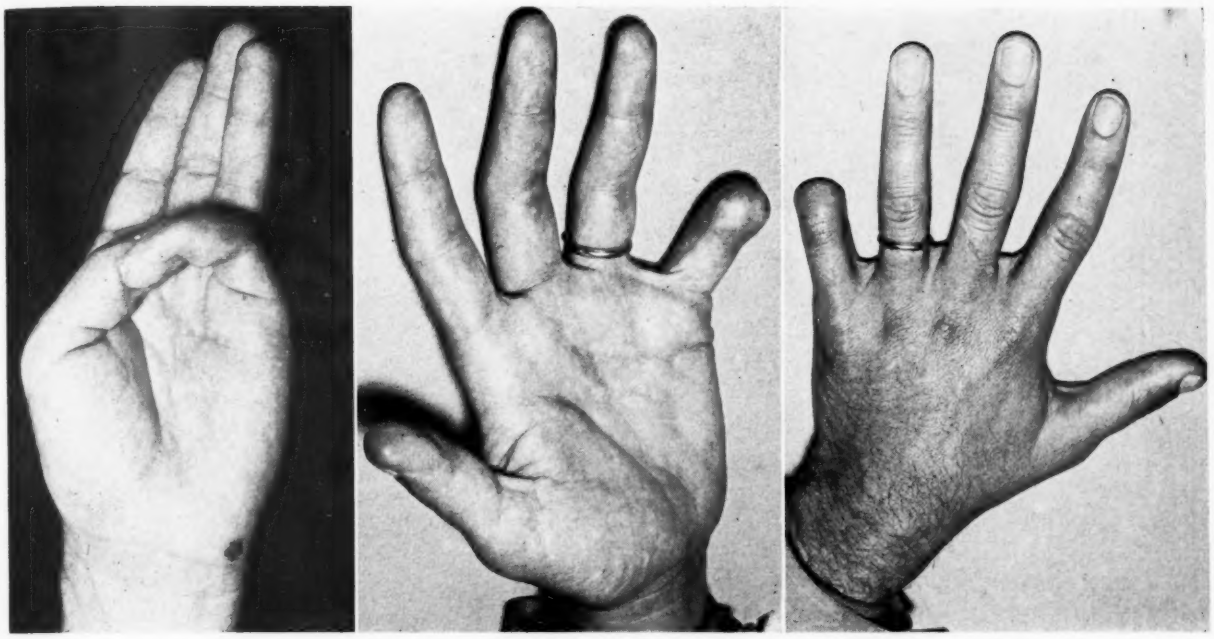
A repair for serious loss of pulp and skin from the palmar aspect of the distal phalanx of the thumb is described and then evaluated in terms of the criteria listed. The result of its application to a patient who was subsequently followed up for ten months is described.

TECHNIC

Brachial nerve block or general anesthesia is preferred. The entire injured hand and forearm are prepared and irrigated in the usual manner. The injured thumb is débrided and covered with saline-moistened gauze. A racket incision is made on the dorsum of the distal phalanx of the fifth finger. The incision starts at the distal interphalangeal joint in the dorsal midline, proceeds distally and encircles the nail and nail bed. With the finger thus split, the distal phalanx is disarticulated with the nail and nail bed. The filleted phalanx is now ready for use as a well vascularized and specialized pedicled graft for the thumb. The hand is placed in the "Boy Scout salute" position, the filleted graft is shaped to fit the defect and a plastic approximation of the edges made.

The hand is dressed and immobilized in the "salute position" (Fig. 1) and kept elevated for a few days. Finger and wrist exercises are started early. Sutures are removed at ten to fourteen days. After two to three weeks the patient is instructed to apply a rubber band tourniquet to the base of the fifth finger. When the graft remains pink indefinitely with the tourniquet in place, the second stage may be undertaken.

At the second procedure the amputation through the fifth finger is completed, the distal end of the reconstructed thumb is shaped and



1 2 3

FIG. 1. The hand as it appeared ten days after the first stage procedure.

FIG. 2. Palmar view of the final result three months after the injury.

FIG. 3. Dorsal view of the final result three months after the injury. More of the fifth finger can usually be saved.

this edge of the graft sutured. (Fig. 2.) Postoperatively only routine care is required.

CASE REPORT

A twenty-six year old engineer injured his left thumb while changing an automobile tire. All of the soft tissue was avulsed from the palmar aspect of the distal phalanx. The periosteum of the phalanx was exposed in the length of the wound. Bone was intact as was the nail bed. No other significant injury was noted. After discussion with the patient, a skilled and intelligent man, the procedure previously described was undertaken. It was technically easy and was quickly performed. (Fig. 1.)

The postoperative course was without incident and primary healing occurred with a fine pliable scar at the periphery of the grafted area. Six weeks after this primary procedure the second stage was performed, and approximately two weeks later the patient had resumed full preoperative activities with satisfaction. In appearance the reconstructed thumb is hard to distinguish from normal. (Figs. 2 and 3.) It has not at any time been tender or dysesthetic and has withstood hard usage without ill effect. Sensation approaches normal.

The process of neurotization has been of particular interest. Within a few weeks there was return of gross sensation. Three months after completion of the second stage of the procedure the patient was examined by a neurological surgeon.* His report in some detail follows:

"Touch: there is no dysesthesia or false localization. There is one area about 3 mm. in diameter on the ulnar side of the graft which is anesthetic and almost totally analgesic. The patient cannot distinguish between paper strip, cotton wisp and wooden splinter stroking over the graft. There is hypalgesia to single pin prick with a rare pain sensitive spot. A summation effect, both spatial and temporal, is present throughout. There is no temperature sense to mild degrees of stimulation. To more marked changes there is sensation after some delay."

Three months later a similar examination was performed by the same examiner. The report follows:

"There is no dysesthesia, false localization or tenderness. Hypesthesia and hypalgesia are present and seem more apparent at the distal than at the proximal end of the graft. Deep pressure sense is normal. The scar is fine and pliable. Patient states that the finger feels essentially normal and has felt so since about one month after the previous examination. His only noticeable disability is in buttoning his shirt collar, an act in which he specifically utilizes the anesthetic portion of the graft.

* Dr. William E. Hunt, Division of Neurological Surgery, Ohio State University College of Medicine.

"Regeneration has probably been from proximal as well as from below. There is not, and has never been, any evidence of Tinel's sign or hyper-reactivity."

COMMENTS

A form of pedicled graft to replace the tactile pad of the distal phalanx of the thumb has been described. Its major use is where massive loss of pulp has occurred, for in such a case cross finger and palmar skin flaps are of no avail while pedicled grafts from the abdomen and elsewhere have disadvantages of abnormal sensation and often poor durability as well as prolonged and awkward immobilization. The following factors should be mentioned in evaluating this repair:

First, the repair tissue is indeed similar to the specialized structure lost and is durable and non-tender.

Second, the utilization of the distal phalanx of the fifth finger does not seem to be a disproportionate handicap. There is, of course, a natural reluctance to sacrifice a portion of a normal finger. In an occasional patient this may be unjustified. In general, however, one has only to consult insurance company and industrial commission evaluations of the thumb and the fifth finger to be reassured. On this basis, if the other characteristics of the repair are advantageous, the sacrifice of the normal phalanx appears to be justified.

Third, neurotization appears to be satisfactory although not perfect. In the opinion of the neurosurgical examiner it was superior to the usual result obtained by other methods of repair.

To quote from Bunnell's classic text [*1*], "In the hand, sensation is equal in value to motion. The hand is a sense organ specialized for stereognosis. This is especially true of the area supplied by the median nerve. The pulps of the thumb and first three fingers are the eyes of the hand. Their rugae furnish separate points of contact for crisper images and the pulps are rich in special touch corpuscles. When we construct a new thumb or finger using pedicle skin from the abdomen, or place a patch of this on the tactile surface of a digit, sensation to distinguish touch or pain will return, but not at all like the quality in normal finger skin that makes for stereognosis. Therefore, whenever possible, it is well in these strategic areas to, by transposing normal skin from the vicinity for pedicle skin, furnish this quality of sensation."

Fourth, the method would appear to involve no risk in excess of other methods which, in themselves, carry very minimal hazard. Immobilization is minimal and the position comfortable and compatible with normal one-handed activity. Finger and wrist exercises may be instituted almost at once.

Fifth, the cosmetic result of the thumb appears to be very acceptable. In this case the appearance is basically normal except for a thin rim of plastic scar. The loss of the distal phalanx of the fifth finger is of course, a cosmetic disadvantage which must be evaluated according to individual esthetic standards.

It would seem then that the repair is advantageous by the usual criteria, but at the cost of the normal distal phalanx of the homolateral fifth finger. These values must be balanced for each patient. When major loss of pulp has occurred it would appear to be well worth while.

SUMMARY

A repair for loss of the distal tactile pad of the thumb is described which seems to offer advantages. The repair tissue and final function are similar to the original tissue lost. Return of sensation is more than usually satisfactory. The repair is suggested for some cases in which major loss of pulp has occurred.

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Triple Primary Cancer

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BILLROTH in 1869 first reported the occurrence of multiple primary malignancies. Since that time reports of multiple malignancies involving separate organs or systems have been quite infrequent.

Warren and Gates [5] outline the following criteria for the diagnosis of multiple malignancies: (1) Each tumor must present a definite picture of malignancy. (2) Each tumor must be distinct. (3) The probability of one tumor being a metastasis of the other must be excluded.

Utilizing these criteria, Watson [6], in a review of 16,626 patients with cancer, found a second malignant tumor in a different organ in 538 patients (3.2 per cent) and a third carcinoma is only eleven patients. Mider et al. [2], in reviewing 3,966 cases, found a second malignant tumor in 179 patients (4.5 per cent) and more than two primary tumors in only ten patients. In 618 cases of cancer of female genitals Marrangoni and McKenna [3] found fifteen multiple tumors (2.4 per cent); in two cases there were triple malignancies.

Barrett et al. [1] in reviewing fourteen series of multiple primary malignancies, found the average interim to be 3.2 years, the longest being fourteen years. The incidence of primary multiple malignancies in these series ranged from .3 to 6.8 per cent. The average age of occurrence varied between 50.4 and 62.1 years. There was a slightly increased incidence in the male.

The following is a case in which three primary malignancies developed over a seventeen-month period. Each malignancy adheres to the criteria as outlined by Warren and Gates [5].

CASE REPORT

This sixty-three year old white man entered this hospital on December 7, 1954, with the chief complaint of a persistent chronic cough of five weeks' duration. This cough was for the most part non-productive but was associated with blood-tinged sputum on several occasions. In addition he complained of increasing weakness and a 10 pound weight loss during the prior six months. Because of these symptoms he consulted his physician. A lesion in the area of the lower lobe of the left lung quite suggestive of a neoplasm was noted on chest roentgenogram and it was therefore recommended that the patient be transferred to this hospital.

Preoperative studies included a proctoscopic examination. At 15 cm. from the anal margin a sessile polyp measuring 1.5 by 2 cm. was noted and excised with biopsy forceps. The base was fulgurated. This polyp was interpreted microscopically as an adenocarcinoma, grade II. In several

FIG. 1. Poorly differentiated adenocarcinoma occurring in a sessile polyp with invasion of the muscularis mucosa.

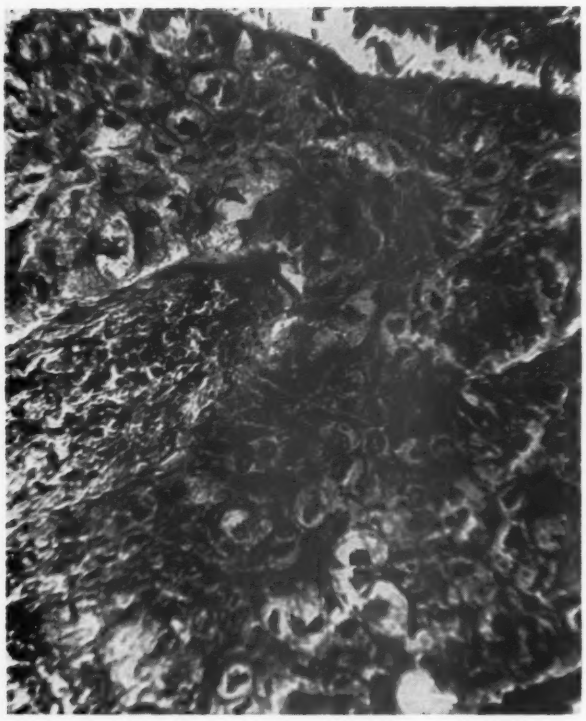

FIG. 2. Bronchogenic carcinoma, squamous cell type, primary in left lower lobe bronchus.

FIG. 3. Melanoblastoma involving retina of right eye. Note marked anaplasia and pigmentation.

areas the basement membrane was disrupted with invasion of the adjacent stroma by tumor cells. (Fig. 1.) A subsequent air contrast barium enema did not show evidence of additional polyps.

On January 7, 1955, a left thoracotomy was performed. A tumor mass approximately 7 cm. in diameter was present in the left lower lobe. There was no gross evidence of metastatic involvement of the hilar nodes. Since the patient's preoperative maximum breathing capacity was only 39 L. per minute, it was elected to perform a lobectomy rather than a pneumonectomy. This tumor was a bronchogenic carcinoma, squamous cell type. (Fig. 2.) The postoperative course was uneventful.

An anterior resection of the colon was discussed with the patient, who was most reluctant to accept a second major operative procedure. Sigmoidoscopic examination performed two months after the original extirpation of the polyp failed to reveal any evidence of its recurrence. In view of the patient's attitude toward further surgery, his very limited pulmonary reserve and the questionable prognosis following the lobectomy for bronchogenic carcinoma, it was elected to follow him up closely at three-month intervals for recurrence of the lesion.

On May 2, 1956, the patient complained of loss of vision in the left eye. The pupil was fully dilated and a large pigmented mass was found extending from the 2 o'clock to the 6 o'clock position within the eye with positive transillumination. The right eye showed no evidence of abnormality. The left eye was therefore enucleated. Microscopic examination confirmed the diagnosis of a melanoblastoma involving the retina.* (Fig. 3.) The patient was last examined in this hospital on September 20, 1958, at which time there was no evidence of recurrence of any of the malignancies.

COMMENTS

There is still a difference of opinion as to the chance of a second primary lesion developing. Warren and Ehrenreich [*4*], following a review of 2,829 cancer autopsies, concluded that the probability of the development of a second primary cancer was increased ten times over the probability of the development of the initial primary cancer. More recent series by both Watson [*6*] and Mider et al. [*2*] indicate that the chance of a separate carcinoma developing in an organ or tissue different from the one first affected is no greater than if the patient did not have one primary cancer.

However, as is demonstrated by this case, the second primary malignancy, or even a third, may occur. Frequently there is a tendency following the treatment of one tumor to

* This neoplasm was treated by Dr. T. H. Willcockson, Yankton, South Dakota, who kindly provided the history and microscopic slide of the lesion.

attribute all future symptoms to its recurrence or spread. Such need not be the case. Another primary neoplasm may be presenting itself and still be amenable to treatment. A patient with a previous history of cancer deserves those investigative procedures necessary to rule out a second or even a third primary lesion.

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"Before long the old forms of traditional philosophic scholarship had begun to be hard pressed by the vigorous intellectualism of the Renaissance. The old order and the new were fighting for supremacy, making the universities, the schools and the churches their battleground. And in the midst of the conflict there grew up one of the first giants of surgical history. His name was Andreas Vesalius and, true son of the Renaissance, he was vigorous in mind and body and as full of intellectual vitality as the age in which he lived. He was not a practicing surgeon, for his interest, his preoccupation, his driving obsession was the study of anatomy. Without a knowledge of anatomy there can be no true surgery, and the work of Vesalius laid the foundation on which the advance of surgery has been built." (From: Young, A. Scalpel: Men Who Made Surgery, p. 9. New York, 1956. Random House.)

SPECIAL DEPARTMENTS

Surgery Court Cases

HOWARD NEWCOMB MORSE,* *Chicago, Illinois*

WICKOFF VS. JAMES

District Court of Appeal of California

324 P. 2d 661

This was a malpractice action against a hospital and a surgeon who tore a patient's intestine during a sigmoidoscopic examination to determine if an entire rectosigmoid polyp had been removed from the large intestine. The Superior Court of Napa County, California, entered judgment dismissing the patient's case, and the patient appealed.

The patient, who was thirty-nine years old, entered the hospital for the purpose of having a rectosigmoid polyp removed from the lower portion of the large intestine adjacent to and immediately above the rectum. The surgeon who performed the operation was an employee of the hospital.

After an operation such as this it is customary to examine the situs of the polyp for the purpose of ascertaining whether or not the entire polyp has been removed. Accordingly, prior to leaving the hospital, the patient was taken to the surgeon's office for the purpose of undergoing the examination.

To examine the situs, the surgeon attempted to insert a sigmoidoscope, ¾ inch in diameter, into the patient's rectum. The examination was unsuccessful because the surgeon was unable to insert the instrument without causing great pain to the patient. It was decided that the examination would be performed at a later date while the patient was under an anesthetic. The patient was discharged from the hospital.

Five days later the patient returned to the hospital for the purpose of undergoing the sigmoidoscopy. She was given a general anesthetic and a sigmoidoscope was inserted into the rectum to the 15 cm. level (5.90 inches) without difficulty. At this point the obdurator was removed because the surgeon desired to pass the instrument under direct vision.

In attempting to advance the sigmoidoscope under direct vision slight difficulty was encountered; visual examination through the instrument showed that a loop of the small intestine was visible. A diagnosis of accidental perforation of the sigmoid wall was made. The patient was immediately taken to surgery where abdominal repair was performed. Immediate action was required because of the danger of peritonitis.

The patient contended that the evidence established a prima facie case of negligence on the part of the surgeon and that the lower court erred in dismissing the patient's case. The District Court of Appeal of California concurred in the patient's contention and reversed the decision of the trial court.

CHAMBERS VS. NOTTEBAUM

District Court of Appeal of Florida

96 So. 2d 716

This was an action by a patient against a surgeon, alleging trespass to the person. The Circuit Court of Dade County, Florida, rendered judgment for the patient, and the surgeon appealed.

The patient suffered from a lame appendix,

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for which he consulted the surgeon a number of times during the summer while attending a university summer school. In the middle of August, while he was out of school for a period of weeks, the surgeon suggested that he have his appendix removed at that time for convenience. There was no flare-up or emergency. When the operation was arranged, on that day in August, the patient informed the surgeon that he would not permit a spinal anesthetic, and the surgeon agreed not to use that type of anesthetic.

After the operation the patient claimed that a resulting permanent injury in the form of a partial paralysis of one of his legs was caused by the use of a spinal anesthetic administered by the surgeon, contrary to his express instructions. The surgeon admitted that a spinal anesthetic was administered but denied that its use caused the injury.

The District Court of Appeal of Florida affirmed the decision of the lower court. The District Court of Appeal declared that a surgeon cannot operate "on a patient without his express or implied consent, or in a manner contrary to the patient's express instructions."

The Diagnostic Corner

A CLINICAL and radiological teaching exercise pertaining to the everyday problem of differential diagnosis of rectosigmoid lesions.

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THE patient was a sixty-two year old white man, an automobile salesman, who had experienced recurrent episodes of cramping pain in the lower part of the abdomen for many years. The pain was located primarily in the lower middle and left lower quadrant of the abdomen, and was aggravated during periods of emotional and physical stress. The patient had taken laxatives for constipation for many years, and was also taking Metamucil® regularly. He had noticed no melena, weight loss, pain on defecation or change in bowel habits. A barium enema examination elsewhere had shown what the referring physician thought to be "diverticulitis," although the possibility of carcinoma led him to send the patient to our institution for surgical evaluation. The only abnormal physical finding was a palpable tender mass 5 by 5 by 5 cm. in the left lower quadrant of the abdomen. There was no rebound tenderness. Intravenous pyelogram showed some obstruction of the lower portion of the left ureter. Hemogram, urinalysis, and serum electrolyte and blood volume studies were normal. A barium enema was performed and the foregoing film clearly demonstrates a lesion in the rectosigmoid colon. The irregular, ragged-appearing lumen did not vary during fluoroscopy or on numerous films.

What is your diagnosis?

Please turn page for answer

DIAGNOSIS

Pseudodiverticulum of the colonic mucosa with acute and chronic inflammation and pericolic abscess formation.

The barium enema film showed a rather long, irregular, narrowed segment of rectosigmoid colon with slight tapering from both ends of the lesion toward an extremely narrow lumen in the center of the lesion. These findings are more characteristic of diverticulitis, or some other pericolic lesion, than they are of malignancy. However, the rather abrupt transition between normal mucosa and the proximal side of the lesion is somewhat suggestive of carcinoma. There were no demonstrable diverticula, whereas in most cases of diverticulitis at least one or two diverticula can be identified in or adjacent to the diseased narrowed segment of rectosigmoid. The clinical story indicated a benign inflammatory lesion because of the long history and absence of weight loss, melena or change in bowel habits. However, the palpable mass in the left lower abdominal quadrant in the face of an x-ray appearance which was nonspecific for either diverticulitis or neoplasm made us believe that surgery was the wisest approach.

At surgery a stony hard sigmoid mass was found frozen to the peritoneum, bladder and other adjacent pelvic structures. The left ureter was not involved, although it was slightly compressed against the left common iliac artery and vein, which accounted for the obstruction of the lower portion of the left ureter seen on preoperative intravenous pyelogram. The mass was slightly smaller than two doubled fists, and it was impossible at surgery to differentiate grossly between carcinoma and inflammatory mass. Frozen section showed no evidence of malignancy but only an inflammatory reaction. The mass was then freed from the surrounding structures by finger dissection and a Baker type of anterior resection was performed. The patient had an uneventful postoperative course and was discharged from the hospital on the twelfth postoperative day without symptoms and having normal daily bowel movements on full diet without laxatives for the first time in many years.

Pathological examination of the gross specimen showed no evidence of diverticula, although an epithelized "pseudodiverticulum" was seen. A marked amount of acute and chronic inflammation and abscess formation surrounded this portion of the rectosigmoid colon. It is postulated by the pathologist that the pseudodiverticulum might represent reepithelization of a sinus tract which may have formed following perforation of the sigmoid by a sharp foreign body. It is of interest that the patient had swallowed a chicken bone some years previously, although he was unable to relate his symptoms to this event.

It is important to remember that the nature of lesions such as this often cannot be determined radiologically before operation, and frequently cannot be determined grossly at surgery. Furthermore, carcinoma and diverticulitis occur in patients in the same age group, and occasionally occur together and involve the same segment of bowel. Surgical removal has resulted in complete relief of troublesome symptoms for the patient discussed herein, and has also removed the fear of carcinoma for the patient, the referring physician, the surgeon and the radiologist.

REFERENCES

1. Schatzki, R. and Hawes, L. E. Roentgenological differential diagnosis between cancer and diverticulitis of colon. *Radiology*, 34: 651–662, 1940.
2. Wigh, R. and Swenson, P. C. Roentgenologic aspects of diverticulitis and its complications. *Am. J. Surg.*, 82: 587–596, 1951.

Book Reviews

The Chemical Dynamics of Bone Mineral. By William F. Newman and Margaret W. Newman. University of Chicago Press. Chicago, 1958.

The physiology of bone, especially its mineralization relative to the homeostatic circumstances of the blood, has been poorly understood. Much of the problem resolves itself in a failure to appreciate the mechanism of calcification in terms of the concentrations and solubilities of Ca and P. In an attempt to resolve this problem the authors review the surface chemistry and solubility properties of the mineral substance of bone. They begin with the fundamental chemistry of solutions and solubilities and relate these to the special environment of Ca and P in serum and bone. They continue with a description of the mineral phase of bone in terms of its chemical morphology. Of special importance for an understanding of the authors' hypothesis of bone mineralization is an appreciation of their discussion of the surface chemistry of the bone crystals and its effects on the deposition process.

In the second half of the book the authors present a discussion of the dynamic state of bone metabolism as it proceeds under the control of known physiological regulators, and conclude with a consideration of the mechanisms of calcifications as influenced by this metabolism. The authors make free use of physical chemistry concepts to present their material.

R. O. Moore, M.D.

Operative Surgery. Volume VI: Hand, Amputations, Plastic Surgery, Gynaecology, and Obstetrics. General Editors, Charles Rob, M.C., M.CHIR., F.R.C.S. and Rodney Smith, M.S., F.R.C.S. 123 pages. Butterworth & Co., Ltd. London, 1958.

Generally this is a very good operative text; however, any attempt to cover so many subjects in one book must of necessity be limited. In all sections the variety of described and illustrated procedures is limited. This is most noted in the sections on the hand and gynecology. On the other hand, the illustrated operative procedures which are described are up-to-date. The written descriptions are concise and clear, and are easily followed with the illustrations provided; however, the illustrations are not outstanding from a purely anatomical viewpoint. Some of the procedures illustrated and described in the sections on the hand and plastic surgery are not used as often or as "routinely" in American Clinics. Some of the gynecological procedures are oversimplified anatomically. Certain time-honored but less often indicated procedures are deemphasized in favor of more commonly used procedures. In summary, this is a good text of operative surgery with clearly written descriptions accompanying only fair illustrations and suffering only from the limitations of forced brevity common to most similar works.

Roger D. Williams, M.D.

Memoirs of a G.P. By Otis Marshall, M.D. First edition, 155 pages. Vantage Press, Inc. New York, 1958. *Price* $3.50.

A brief account of the boyhood and fifty years of general practice of a Virginia physician. It is a pleasant and modest but unexciting record. One gains the impression of a thoroughly decent and sincere person and a conscientious and realistic practitioner. Basically, however, there will be little to excite the medical reader and basically no new aspects of the history of practice in this country are presented.

Robert N. Watman, M.D.